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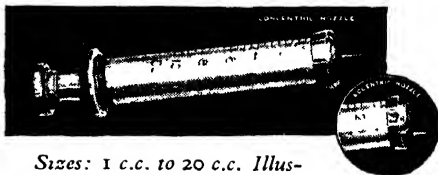
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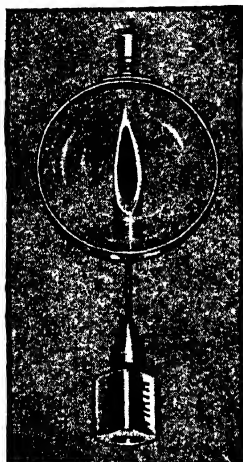


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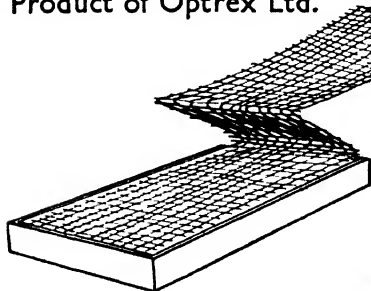
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CONTENTS

PART I—CRITICAL SURVEYS

PUBLIC HEALTH IN THE PRESENT WAR - - - - -	PAGE 1
SIR ARTHUR S. MACNALT, K.C.B., M.D., F.R.C.P., F.R.C.S. Editor-in-Chief of the Official Medical History of the Present War; formerly Chief Medical Officer of the Ministry of Health and the Board of Education	
SURGERY - - - - -	13
G. GREY TURNER, LL.D., D.Ch., M.S., F.R.C.S., F.R.A.C.S., F.A.C.S. Professor of Surgery, University of London; Director of Department of Surgery, British Postgraduate Medical School, London	
OBSTETRICS AND GYNAECOLOGY - - - - -	22
JAMES YOUNG, D.S.O., M.D., F.R.C.S.Ed., F.R.C.O.G. Professor of Obstetrics and Gynaecology, University of London; Director of Department of Obstetrics and Gynaecology, British Postgraduate Medical School, London	
- - - - -	
ALIMENTARY TRACT DISEASES - - - - -	30
SIR ARTHUR HURST, D.M., F.R.C.P. Consulting Physician, Guy's Hospital, London	
BACTERIOLOGY - - - - -	37
C. H. BROWNING, M.D., LL.D., D.P.H., F.R.S. Gardiner Professor of Bacteriology, University of Glasgow; Director, Laboratory of Clinical Pathology, Western Infirmary, Glasgow	
ENDOCRINOLOGY - - - - -	44
ALLAN W. SPENCE, M.D., F.R.C.P. Assistant Physician, St. Bartholomew's Hospital, London	
ACUTE INFECTIVE DISEASES - - - - -	57
WILLIAM GUNN, M.B., Ch.B., M.R.C.P., D.P.H. Medical Superintendent, North-Western Fever Hospital (L.C.C.)	
DISEASES OF THE LUNGS - - - - -	66
MAURICE DAVIDSON, D.M., F.R.C.P. Physician, Hospital for Consumption and Diseases of the Chest, Brompton; Consulting Physician (for Diseases of the Chest) to the London County Council; Honorary Visiting Physician, Papworth Village Settlement, Cambridge	
MENTAL DISEASES - - - - -	72
R. D. GILLESPIE, M.D., F.R.C.P., D.P.M. Physician in Charge, Department of Psychological Medicine, and Lecturer in Psychological Medicine, Medical School, Guy's Hospital, London; Air Commodore, R.A.F.V.R.	
THE AUTONOMIC NERVOUS SYSTEM - - - - -	81
J. R. LEARMONTH, Ch.M., F.R.C.S.Ed. Professor of Surgery, University of Edinburgh	

NEUROLOGY - - - - -	PAGE 87
J. PURDON MARTIN, M.D., F.R.C.P. Physician, National Hospital for Nervous Diseases, Queen Square; Neurologist, British Postgraduate Medical School, London	
DISEASES OF THE PROSTATE GLAND AND BLADDER - - -	92
KENNETH WALKER, O.B.E., M.B., F.R.C.S. Surgeon to the Genito-Urinary Department, Royal Northern Hospital, and to St. Paul's Hospital, London	
TROPICAL MEDICINE - - - - -	96
SIR LEONARD ROGERS, K.C.S.I., LL.D., M.D., F.R.C.P., F.R.C.S., F.R.S. Late Physician, Hospital for Tropical Diseases, London	
VENEREAL DISEASES - - - - -	102
BREVET-COLONEL L. W. HARRISON, D.S.O., M.B., Ch.B., F.R.C.P.Ed. Technical Adviser in Venereal Diseases, Ministry of Health; Consultant in Venereal Diseases, British Postgraduate Medical School, London	

PART II—DRUGS

RECENT DEVELOPMENTS IN DRUG THERAPY - - - - -	109
W. J. DILLING, M.B., Ch.B. Professor of Pharmacology and General Therapeutics, University of Liverpool	

PART III—ABSTRACTS

ABDOMINAL PAIN AND ACUTE ABDOMINAL EMERGENCIES—YELLOW FEVER - - - - -	119
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CUMULATIVE INDEX

INTRODUCTION

BY

THE GENERAL EDITOR

The general plan of the Annual Medical Progress Volume to the *BRITISH ENCYCLOPAEDIA OF MEDICAL PRACTICE* has been mainly followed in this, the fifth of such Volumes. As before, this volume is divided into three parts, which contain respectively a series of critical surveys of various branches of Medicine, a section dealing with new developments in drugs, and abstracts from current medical publications. I should like to acknowledge again my indebtedness to the Publishing Editor, Dr. D. Hay Scott.

PART I—CRITICAL SURVEYS

This consists of a series of authoritative signed reviews dealing in general terms with the present position of some branches of medical science and practice, and indicating the possible future developments in these. The subjects dealt with in these critical surveys will vary from year to year according to the circumstances of medical progress. The *Encyclopaedia* is much indebted for the help given in these difficult times by the contributors of these surveys.

PART II—DRUGS

In this section new drugs, or modifications of existing drugs, are discussed from their therapeutical and pharmacological aspects, and it is a pleasure to express high appreciation of Professor W. J. Dilling's help.

PART III—ABSTRACTS

This section brings together the essentials of a large number of papers published throughout the year ending 30th June, 1943, by British, American and other authors. As a result of the wide extent of the War the output of European journals and other medical publications has greatly diminished, but the supply from North America has so far been well maintained. Much care has been bestowed on the selection of these abstracts, which are arranged as far as possible on the same plan as that adopted in the parent *Encyclopaedia*. The material in this part contains the results and opinions of the authors of the abstracted papers, but it is not suggested that all these will be finally accepted by the medical profession.

Since October 1942, in order to minimize inconvenience and to give subscribers information as early as possible, an Interim Supplement consisting of five main subjects, each with four or five relative abstracts and a signed editorial commentary, has been issued. The abstracts and commentaries which have appeared up to the time of going to press are included in Part III of this volume.

THE CUMULATIVE INDEX

A Cumulative Index to all previous Annual Volumes to the *Encyclopaedia* and therefore covering the period 1939-44 is included at the end of this volume.

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PUBLIC HEALTH IN THE PRESENT WAR

By SIR ARTHUR S. MACNALT, K.C.B., M.D., F.R.C.P., F.R.C.S.

EDITOR-IN-CHIEF OF THE OFFICIAL MEDICAL HISTORY OF THE PRESENT WAR, FORMERLY
CHIEF MEDICAL OFFICER OF THE MINISTRY OF HEALTH AND THE BOARD OF EDUCATION

HISTORY

In every war of which we have records, from the days when Sennacherib invaded Judah onwards, the wastage from disease has outnumbered many times the losses that have been incurred from killed and wounded. Disease is a cause of inefficiency in an army and entails vast expense upon the country; it took, however, considerable time for military authorities to learn this lesson. In former days when military hygiene was either non-existent or was in its infancy, the incidence of and mortality from disease among troops on active service must have been extremely high. Sir John Pringle began hygienic reform for the British Army but it needed the Crimean War, during the first winter of which 'the number of men who were disabled by preventable disease amounted to more than one-third of the whole strength of the Army which went out of England', to awaken public concern. The experience of the comparative healthfulness which obtained as soon as the Government Sanitary Commission's recommendations (1855) had been adopted stands on record as being among the great lessons of military hygiene and, with the work of the Commission and of Florence Nightingale on the organization of the Scutari hospitals, made insistent the great work of Army medical reform, which reaped its reward in the medical triumphs and prevention of disease in the war of 1914-18. The issue does not only concern the importance of preventing disease in combatants and the treatment of military casualties in relation to military objectives. In war it is obvious that health among troops diminishes the risk of disease in the civil population with which they are in contact, that disease in civil populations adversely affects the health of troops, and that similarly both military and civil authorities are interested in the maintenance of the public health.

In the war of 1914-18, when a hitherto unparalleled effort was called for to provide a national army, the Local Government Board (then the Central Health Authority) early appreciated its responsibilities in the directions already indicated, and a co-operative organization for the maintenance of public health conditions was arranged between the military and civil health authorities. Recalling the anxious and difficult months of 1914, there is not any doubt that the work of the medical department of the Local Government Board and of the medical officers of health of local authorities saved thousands of lives and prevented much invalidity and sickness among the Forces. Camps were being hastily improvised and were often planned without due attention to full sanitary amenities, they were filled with ardent volunteers, youths from Highland glens and from Yorkshire dales, who were not immune to zymotic diseases and other infections. In the prosaic work of providing water supplies, means of sewage and refuse disposal for camps, isolation hospitals and hygienic billets, the civil authorities helped to conserve man-power and shared in the making of armies. The Army authorities were not unmindful of such assistance. The Army Council stated that the civil cooperation in the unprecedented circumstances of the first eight months of the war was 'invaluable in safeguarding the health of the Forces and in preventing the spread of infective diseases'. Throughout the war many special problems arose in which cooperation was needed and was secured between civil and military health authorities. The picture of civil health in the war of 1914-18 was not wholly unsatisfactory. There was a rise in tuberculosis, a high mortality from cerebrospinal fever, a few cases of malaria and some of dysentery; the war brought its new diseases—trench nephritis, trench fever and encephalitis lethargica (epidemic encephalitis)—but apart from the pandemic of influenza in the winter of 1918-19 the record of public health was good.

The war itself saw the early years of those personal health services which have done so much within the last thirty years to improve the health of the community.

School caterers and the School Medical Service had begun their beneficent work in 1907; the Insurance Medical Service began in 1912. Tuberculosis schemes were being organized in 1913 and 1914, and two important health services, Maternity and Child Welfare and the Venereal Diseases Service, were directly inspired by the war. In the war of 1914–18, therefore, the Public Health Service had a stern apprenticeship to war duties. It cooperated fully and efficiently with the Forces; it was on the alert to deal with epidemics and war-time diseases; and, at the same time, it maintained environmental hygiene, began new health services and, with depleted staffs, looked after the health of the civil population.

Important and extensive as public health responsibilities were during that period they are vastly increased in the warfare of today. It will be interesting for the future historian to trace the evolution of the civil arm and particularly of organized Medicine in warfare, a process which has culminated in the present great organization. There are unprecedented demands now being made on the national health services in war-time. Since the war of 1914–18 the discoveries of science have placed more powerful weapons of destruction in the hands of men. The aeroplane can fly immense distances, bearing death beneath its wings. The enemy makes ruthless attacks upon civil populations. The cities of our land are not any longer 'cities of refuge' for invalids, women and children but may become the most vulnerable centres for attack. With these fateful considerations in mind the Ministry of Health had to take important measures of protection, as well as to maintain the public health services and adapt them to war-time conditions. One such measure was the organization of an emergency medical service, in itself a stupendous task; another was the evacuation scheme which included the evacuation of school children (in collaboration with the Board of Education), expectant mothers, young children, cripples and blind persons from urban centres, and the arranging for their reception in other areas.

PUBLIC HEALTH AT THE OUTBREAK OF THE PRESENT WAR

The vital statistics for England and Wales for the year 1939, despite the inclusion of four months of war, bore witness to the improvement in the public health which had been continuous in recent preceding years. The chief features may be summarized as follows.

- (1) The birth rate was 14·9 as compared with 15·1 in 1938.
- (2) The crude death rate was 12·1 as compared with 11·6 in 1938. The slight rise was probably due to the severe weather in the latter part of the year which favoured respiratory diseases, and to the fact that the proportion in the population of older persons who reach the allotted span of life is increasing from year to year.
- (3) The infant mortality rate (that is the death rate of infants under one year of age per thousand born) was 50; this was again the lowest rate ever recorded, the rate for 1938 which had until then this proud distinction being 53. The figure reflects credit on all who were concerned in the maternity and child welfare services, and on those who were responsible for the evacuation scheme and the care of children in the reception areas.
- (4) The maternal mortality rate declined also to a new low record; it was 2·82 per thousand total births as compared with 2·97 in 1938. The rate from puerperal sepsis was 0·74, and from other causes 2·08 per thousand total births. The year which showed such a satisfactory result in the saving of the lives of mothers had seen the continuation and intensification of effort in maternal welfare. This record figure was particularly satisfactory in view of the phenomenal events which occurred after the outbreak of war.
- (5) Mortality from tuberculosis was not disquieting. The crude death rate from tuberculosis per million living was 636 as compared with 635 in 1938, which are the lowest figures yet recorded. The nation at the outbreak of the present war was therefore fortified by better physique and better health, the gifts of medical and public health progress.

Early plans

Si vis pacem, para bellum. The health services of Great Britain were mindful of the Latin adage and in circumstances of great difficulty did their best to prepare for safeguarding the health of the community and for ensuring provision for the reception and treatment of casualties in the event of war. At the same time the existing health services were maintained and developed and a new service, the Cancer Service, was

established by the Cancer Act of 1939. The Home Office first made open preparations by organizing anti-gas measures and by instructing the public in precautions against aerial gas attack. Local Authorities began to make some provisions for casualty hospitals. The British Medical Association in 1937 began to compile a register of every doctor in Great Britain, in terms of individual desire and aptitude for medical services in the Forces, or for home defence or civil work. Thus at the outbreak of war a complete record of the whole medical profession was ready, together with machinery, in the form of a Central Emergency Committee and local emergency committees. These were then reconstituted as Central and Local Medical War Committees respectively. The Government entrusted to the Central Medical War Committee, in association with the Committee of Reference of the Royal College of Physicians and Royal College of Surgeons, the allocation of doctors to the Forces according to the demands of the latter. Other ways in which the increasing demand for doctors is being supplemented are by the recognition of suitably qualified foreign medical practitioners and, until the United States of America entered the war, by the assistance of many American volunteer doctors.

PRELIMINARY WORK IN WAR ORGANIZATION

For two years previous to the outbreak of the present war the Ministry of Health and its officials worked for long hours and at high pressure, preparing for the threatened ordeal. As the war clouds in Europe gathered and thickened there was an ever-increasing strain upon the Department. Early in 1939, under my direction, a medical organization was set up in five regions of England by a redistribution of part of the existing staff of the Ministry of Health; at the head of each region is a principal regional medical officer, such an organization had been for many years in force in Wales. Although functioning now for war service, there will be many advantages in peace-time in having a permanent public health regional organization directed from the Ministry of Health and in close touch with the local authorities of England. The Public Health Regional Organization works with the Regional Hospital Organization, which is described below. In 1938 I was appointed Chairman of two important Government committees. The first dealt with the problem of emergency hospitals, the second with the recruitment of nurses. The subject of emergency hospital organization for air-raid casualties was a very difficult one because, as has been pointed out, the conditions of modern warfare are so dissimilar from those of the war of 1914-18 that we had not any precedents or experience to guide us. Something had been learned from the aerial bombardments in China and in Spain, but the circumstances in Great Britain made it likely that warfare here would be on a different scale. The estimate of anticipated air-raid casualties was so high that it was obvious it would be an impossible task, in the time available, to make adequate provision for them. I therefore suggested at the outset that the existing hospital provision in Great Britain should be ascertained, and that steps should then be taken to expand and to supplement it as far as was possible; this suggestion was adopted by the Committee. A number of other recommendations were made, the most important of which was that the Ministry of Health should direct the whole Emergency Hospital organization in England and Wales. The Committee's report was accepted in full by the Government and work was then begun to implement the recommendations.

The recommendations of the Nursing Committee led to the following plans. With the help of representatives of the General Nursing Council, Royal College of Nursing, Order of St. John of Jerusalem, British Red Cross Society and others, a Central Emergency Committee for the nursing profession made arrangements for the registration and recruitment of trained or partially trained nurses who were available for service in war-time, and so the Civil Nursing Reserve was established. This was later incorporated in the Ministry of Health, the Central Emergency Committee being replaced by an Advisory Council under the chairmanship of Miss Florence Horsbrugh, Parliamentary Secretary to the Ministry. There were numerous other activities planned and organized by the Government and by the medical profession during this period, for use in the event of war. Some of these are mentioned in the next section but many have had to be omitted because the full story cannot yet be told.

THE EMERGENCY MEDICAL SERVICE

Organization and operation

The main aim of this vast organization is to keep the service in being with powers of

speedy expansion to meet the demands of air-raid casualties. Its main features are as follows.

Regional organization.—In each region a hospital officer or officers appointed by the Ministry of Health is in charge of the hospital scheme and in cooperation with the local authorities.

Central organization.—Centrally a special Department of the Ministry of Health has been set up to deal with air-raid precautions. On the lay side there is a Principal Assistant Secretary with Assistant Secretaries, Principals and clerical staff. On the medical side there is a Director-General of Medical Services with a staff of Medical Officers. This Emergency Medical Services department directs and organizes the hospital services. The hospital medical officers in the different regions are concerned with the details of the work. The liaison with the Local Authority hospitals is easily effected through the medical officers of health of counties and county boroughs.

Planning and development.—Briefly the scheme consisted in the coordination of all hospital services on a wide regional basis. Hospitals were classified according to the facilities they afforded, and were affiliated into sectors, hospitals in the more vulnerable zones being linked with hospitals in safer areas. Each group of hospitals was placed under the supervision of a Group Officer who is responsible for the adequate staffing of all the hospitals in the group, and also for directing the movement of patients between hospitals. London presented a special problem on account of its size and its vulnerability from the air, and the London area—including the contiguous areas of Essex, Hertfordshire, Buckinghamshire, Berkshire, Hampshire, Surrey, Sussex and Kent—was divided into ten sectors, each under a Group Officer. Headquarters were established in the outer part of each London sector, from which all movements of patients from one hospital to another are controlled. The scheme made provision for the necessary number of casualty beds by transferring civil patients to other hospitals or by sending home patients who were fit to travel, by increasing the number of beds and by providing additional accommodation. Accommodation for casualties was augmented by the provision of huts which were capable of taking 44,000 beds. Certain hospitals were equipped by the Ministry of Health to render them more suitable for the treatment of casualties. Convalescent hospitals and homes for the recuperation of patients were included in the scheme. A central organization was set up to arrange with manufacturers for increased supplies of hospital equipment. The medical staff of the Emergency Medical Service at first consisted of the existing medical staffs of the hospitals, necessary additions or replacements of staff being made through the Central Emergency Committee. The nursing needs are met from existing nursing staffs of the hospitals, supplemented by the Civil Nursing Reserve.

Provision for military sick and casualties.—The Emergency Medical Services scheme provides for the military sick patients and casualties as well as for air-raid casualties. The Royal Navy and the Royal Air Force provide for their own sick and wounded but, as the war has proceeded, additional beds have been made available in civil hospitals for naval sick and casualties and, wherever necessary, for some Royal Air Force casualties.

Provision for other classes of patients.—In addition to looking after air-raid casualties and Forces cases, the Emergency Medical Service undertakes primary responsibility for persons suffering from war service injuries (that is for Civil Defence workers and members of the Home Guard who have been injured in the course of their duty by other than enemy action); for sick persons transferred from hospitals in the urban areas, either to make accommodation available for casualties or because accommodation has been reduced by damage or for fear of damage; for unaccompanied children evacuated to reception areas under the Government evacuation scheme and for other evacuees, whether they are billeted according to the Government scheme or make their own arrangements; for whole-time Civil Defence workers and workers in essential industries, transferred from home; and for certain other miscellaneous classes of persons which it has been decided to admit to the scheme. The scheme of the Emergency Medical Services planned before the present war began was thus ready for action when war came. It has been subsequently developed and expanded, with the experience of hostilities. It coordinates the existing municipal and voluntary hospitals into one service and augments their facilities, without impairing their usual peace-time responsibilities. Team work is arranged to meet war-time conditions. In a democratic country so comprehensive an organization could be effected only through the willing coopera-

tion of the voluntary and municipal hospitals and their medical staffs. A grateful tribute must be paid to the hospital authorities for the services they have rendered and are continuing to render to the public weal.

Ambulance services, first-aid posts and laboratories

Other features of the preparation for war emergency were the air-raid ambulance services, the provision for first aid and the laboratory services. An ambulance service for conveying air-raid casualties to first-aid posts and hospitals was organized by local authorities before the outbreak of war. The Ministry of Health also directly organized an inter-hospital ambulance service by the conversion of motor omnibuses and coaches into ambulances. Other ambulances were provided and were maintained by the generosity of American societies, the Home Ambulance Service of the Joint War Organization of the Red Cross Society and the Order of St. John of Jerusalem and by the London County Council. Auxiliary evacuation trains had been assembled by the railway companies according to specifications agreed with by the Ministry of Health before the war. For dealing immediately with casualties in air-raids, fixed and mobile first-aid posts and first-aid points have been established. The first-aid post is planned by and is under the control of a local medical practitioner; it is staffed by trained nurses and auxiliary nursing staff.

Laboratories.—The Medical Research Council has set up a comprehensive laboratory organization throughout Great Britain. The Ministry of Health collaborated closely and linked it up with the public health and hospital organization and with the work of county and municipal laboratories. Depots for the storage of calf lymph, vaccines, serums and blood for transfusion have been established in different parts of the country.

Subsequent developments

The early months of the war.—In September, 1939 at the outbreak of war, the medical and nursing staffs took up their posts in the hospitals and awaited the *blitzkrieg*. But during the subsequent months, before the invasion of Holland and Belgium there were relatively few casualties, and since heavy raids did not appear to be imminent many of the vacated beds were used again for civil sick, for evacuated children and for sick and injured members of the Forces.

The evacuation from Dunkirk.—When the British Expeditionary Force was evacuated from Dunkirk in May and June, 1940 the Emergency Hospital Service dealt for the first time with a large number of wounded. Hospitals on or near the south-east coast were used as casualty receiving stations from which patients, after initial treatment, were conveyed by ambulance trains to hospitals in or near to London and in the west and midlands.

The period of intensive air-raids.—The Battle of Britain lasted from the 3rd of August to the 31st of October, 1940, during which time the country was exposed to intensive daylight air-raids, and the Channel ports were cleared of large numbers of sick persons and others. At the same time there were numerous air-raid casualties. Thereafter the enemy resorted to night bombing, and heavy attacks were made upon London and other large cities. This phase lasted until about May, 1941, and for the rest of the year there was a comparative lull in air-raids on Great Britain. Throughout the period of intensive air-raids the Emergency Hospital Organization was severely tested; it had been designed principally to deal with air-raid casualties, and to provide for an out-flow of wounded from receiving hospitals in the dangerous areas to hospitals at the periphery, and to other hospitals still more remote. In practice the method proved very successful. As an example, in one heavy raid on London in the spring of 1941, all but a few of the patients had been operated upon or had been otherwise treated and removed to peripheral hospitals by the afternoon of the day after the attack. The emergency hospitals were also used to a large extent in the autumn of 1940 to accommodate chronic sick persons who were found in shelters and in rest centres in the London area, and for people who needed to be evacuated from the coastal areas in view of the possibility of invasion.

COMMENTARY

It will thus be seen that the Emergency Hospital Organization is not a static scheme. It has been far from perfect. In the light of subsequent events it can be seen that many mistakes were made, many unnecessary plans were devised and there was much waste

of effort in preparing for eventualities which did not arise. Such defects were almost inevitable in a new organization, and were certainly inevitable in a war which has taken a course different from that of the campaigns of the past. The Emergency Medical Service is constantly being adapted to changing circumstances, and is always faced with new difficulties and with problems to solve. Yet it works. Its success is due to careful central planning, to continual overhauling of the machine and, above all, to the loyal cooperation and work of doctors, students, nurses and hospital workers of every kind. A high tribute must be paid to the efficiency of the ambulance service and to the courage, zeal and resourcefulness of the drivers, many of whom were young women. Countless epic stories are related of their heroism and exploits. Some died at the wheel; others carried on when wounded, thinking not of themselves but of the patients they were conveying to hospital. All were imbued with the spirit of patriotism and self-sacrifice.

THE EVACUATION SCHEME

Medical and health services

Some brief reference may be made to the medical aspect of the subject of evacuation of the civil population. The pre-arranged plans for evacuation which were made by the Ministry of Health and the Board of Education concerned school children, younger children with their mothers, expectant mothers and some other priority classes of the population. Plans were made in England and Wales for the evacuation of 3,000,000 persons; some 1,230,000 persons took advantage of the offer. The scheme was carried out at the beginning of the war on voluntary lines and proved a triumph of organization. In London alone half a million children had to be evacuated. A tribute is due to the whole-hearted way in which local authorities, education authorities, medical officers of health, school medical officers, school teachers and the general public cooperated in the scheme. It is not always appreciated that the moving of so large a proportion of the child population and of others from one portion of England and Wales to another entailed considerable and far-reaching planning and organization, for the work was begun only when children and expectant mothers had arrived at their billets. A heavy additional strain was thrown upon the national medical and health services. With the influx of a large population to portions of the country which were previously rural and were comparatively isolated, local authorities had to make increased provision for water supplies, sewerage, drainage, accommodation for cases of infective disease, maternity hospital accommodation, midwives and so forth. Expansions of the school medical and nursing services were necessary. Medical officers of health had also to consider the future demands that such increase in population would make upon the local health services, for example child welfare clinics and tuberculosis dispensaries, and there was all the additional planning concerned with the health and welfare service of children. Sick bays were established in many areas and a medical service, consisting chiefly of local general practitioners, looked after unaccompanied children in billets. Much of this emergency organization was helped by the advice of the principal regional officers of the Ministry of Health. Extra maternity accommodation and staff was a problem for special consideration and, on the recommendation of the Royal College of Obstetricians and Gynaecologists, the Minister appointed honorary obstetric consultants in the different regions, to advise him on this subject. Greatly increased demands were indeed made upon all the social services.

Nurseries and camps

Certain special arrangements made in reception areas may be mentioned. Residential nurseries have been provided for the reception and care of children under five years of age, emergency maternity homes have been set up in various parts of Great Britain, hostels have been provided for children needing special care and supervision, and special hostels accommodate families who cannot readily be billeted in the ordinary way. Thirty camps, twenty-two of them being privately-owned holiday camps, eight of them National Council of Social Service or Y.M.C.A. camps, were occupied (with one exception) by handicapped children—the deaf, the crippled, patients with heart disease and mental defectives—who could not reasonably be billeted in private houses, either in the interests of the children themselves or in those of householders.

School children and refugees

The normal work of the School Medical Service was considerably dislocated, the

medical officers and school nurses being employed in cooperating with the medical and nursing staffs of reception areas in the reception and medical examination of evacuees. Subsequently the normal activities of the Service in the inspection and medical care of school children were resumed as far as possible both in evacuation and in reception areas. There has been a great increase in the provision of school meals and of milk.

In the early part of 1940 a new plan provided for the registration of school children by their parents, on the understanding that the children would not be evacuated until bombing on land began. The response was less than had been anticipated, and in the reception areas there was a drift back of some of the children to their homes. The occupation by the enemy of Norway, the Low Countries and northern France brought the risk of sea-borne invasion; the native population of certain coastal areas was reduced by an organized evacuation of school children, and non-essential residents in some areas were persuaded to leave without resort to the Government's compulsory powers for evacuation of the coastal and inland towns. When heavy bombing began in September, 1940 the evacuation of children from London was accelerated and by the end of March, 1941 large numbers had found shelter in reception areas. Further efforts were made to disperse the London population, for example free travel vouchers and billeting certificates were made available for those evacuated under arrangements privately made, for mothers with children of school age or under, for expectant mothers at all stages of pregnancy and for aged, infirm, blind or invalid persons. These provisions were later extended to people in provincial areas and were used by many. Additional pressure was put on the evacuation scheme by refugees from France and the Low Countries, from the Channel Islands and from Gibraltar. Some of these evacuees have been accommodated within the framework of the billeting schemes of local authorities, and others have been housed in self-contained colonies.

COMMENTARY

It is not surprising that in the national game of 'general post' misfits occurred, and that concern was expressed at the low standards of cleanliness and conduct found in certain of the evacuees, but blame for such things should not be assigned to the inadequacy of the public health and school medical services; they are rather arguments for the increased support and extension of such services. The Annual Reports of the Chief Medical Officer of the Board of Education for years have recorded the state of cleanliness of school children, have noted improvement and have deplored the degree of uncleanness which still persists; in some districts it is necessary to cleanse children several times in the course of a year. The root cause of such deplorable conditions lies in the home of the child; such conditions show that slum clearance has not yet gone far enough, that low standards of living still persist and that the lessons taught in the school and clinic sometimes fail to reach the older generation.

Evacuation stands on record as a great social experiment which was performed successfully, but its main object was only partially achieved. As the weeks passed and the urban centres of Great Britain remained free from air-raids, family ties prevailed despite good advice from persons in authority, and many children and wives returned to their homes in the towns. The number of persons who had returned by 8th January, 1940 was estimated to be about 675,000. The drift home was unfortunate but inevitable in the absence of compulsion. But, as with the Emergency Medical Service, the Government scheme should not be condemned because events have pursued a path different from the one expected. Who can say that the policy of preparing for casualties and for the evacuation of children, expectant mothers and others was not preventive medicine *in excelsis*? Some indication of this is given by the low rates which prevailed of the common infective diseases. The evacuation scheme will always rank as one of the greatest health and social experiments designed by a government to protect children as far as possible from the horrors of aerial bombardment. Evacuation, unfortunately, cannot protect every child from battle, murder and sudden death when indiscriminate warfare is a weapon of the enemy. The essence of the scheme is that it disperses children from congested centres over the countryside and thereby minimizes the danger. The planning and arrangements proved successful; the system has grown and developed as the result of experience. Highest reward of all, the urban child has benefited in mental and physical well-being by the change to a rural and open-air environment, and the serious epidemics which were dreaded have not occurred,

AIR-RAID PRECAUTIONS

Gas attack

Up to the time of writing poison gas has not been used by the enemy, but precautions have been taken against the threat. The Ministry of Home Security is responsible for general advice to the public, for the provision of respirators and for the decontamination services of local authorities. The Ministry of Health supervises arrangements made by these authorities for cleansing persons exposed to 'blister gas' and for decontamination of clothing. A large number of cleansing stations have been constructed at first-aid posts and mobile cleansing units are provided. Provision is made at Emergency Medical Service Hospitals for the decontamination of gassed stretcher cases. The public were asked at first always to carry their respirators but, in view of the rubber shortage and in order to keep the respirators in good condition, this instruction was relaxed in 1942 until the possibility of gas attack should seem more imminent.

Care of the homeless

In order that persons rendered homeless by enemy action should be cared for during the air-raids, a large number of buildings were converted into rest centres and were suitably equipped by public assistance authorities and by voluntary organizations. Information centres were set up for the guidance of homeless persons. Dormitory facilities have been added to rest centres and large hostels consisting of huts have been erected outside the principal centres to give temporary accommodation until billeting can be arranged. Hostels have been provided for the aged and infirm, and stocks of clothing have been collected and canteens provided.

Air-raid shelters

The policy of the Government had been to disperse the population as much as possible by providing a small domestic shelter, namely the Anderson shelter, which could be erected near the dwelling-house. A certain number of public brick shelters were provided by Local Authorities, but there were few underground shelters. Provision of shelter dormitories was not at first contemplated; when heavy and prolonged air-raids came at night, people resorted in large numbers to public shelters, to the underground railways and to underground store depots, especially in London, which bore the brunt of the night attacks. There was much congestion and overcrowding, lack of adequate ventilation, insufficient sanitary accommodation and other hygienic defects. The problem of safeguarding the health and comfort of the shelterers became urgent. A committee under the chairmanship of Lord Horder was set up to advise on the conditions of air-raid shelters, with particular reference to health. The committee's recommendations were adopted and immediate steps were taken to improve conditions. Sleeping-bunks were installed, and heating, lighting and washing facilities, drinking-water and sanitary accommodation were provided. Damp conditions were remedied. A scheme for the medical inspection of shelters by the public health staff of local authorities was put into force; first-aid posts were established and medical practitioners and nurses were employed to work in the shelters. Restrictions were placed on the number of persons to be admitted to the public shelters used as dormitories, and admission by ticket for habitual users was instituted. More public shelter accommodation was provided, including additional underground accommodation. Local authorities have cooperated with voluntary organizations to safeguard the welfare of shelterers. It was feared that epidemics might originate in the public shelters during the winter of 1940-1; they did not and it is to be hoped that, with the supervision which was instituted and with the improvements effected generally in shelters throughout Great Britain, the shelter population will remain protected from serious outbreaks of infective disease.

HOUSING AND ACCOMMODATION

Day nurseries

The movement to establish nursery schools and day nurseries for children under five years of age has received a great impetus because of the war. Great Britain's needs and those of the U.S.S.R. have caused an increased demand for women workers in armament factories, and the children of such workers must be safeguarded during their mothers' working hours. The Government defrays the whole cost to local authorities for establishing and maintaining the nurseries, which are placed in evacuation and neutral areas as well as in reception areas. For the care of the children more workers are being trained and the Ministry of Health pays the cost of training.

Housing of the people

The outbreak of war put an end to new housing activities except those concerned with houses for war workers. Local authorities now chiefly concentrate on the repair of houses damaged by bombardment. The supply of labour has been limited and certain authorities have devised schemes of mutual aid. When heavy attacks have inflicted damage beyond an authority's resources, the Government has supplied material and labour. As a result of the complete destruction of many houses there has been inevitable overcrowding in some areas; local authorities limit this as far as possible in the interests of public health.

INDUSTRIAL HEALTH

During the present war the problems of the effects of long working hours at continuous high pressure, and of exposure to dangerous substances have again demanded consideration. The Ministry of Labour and National Service—by the Factories (Medical and Welfare Services) Order, 1940—has required occupiers of armament factories to appoint, if requested by an inspector of factories, whole-time or part-time medical practitioners, nurses and welfare supervisory officers. The Ministry of Supply has appointed full-time medical officers in certain factories to give medical supervision to workers whose health is especially liable to be affected by exposure to dangerous substances. In various ways the health of the industrial worker is safeguarded but there is still need for the more comprehensive development of industrial health services. The report of a committee of the British Medical Association (1941) points out that medical supervision of the workers in a factory has a wide meaning. 'Such supervision implies the care of the individual worker in his industrial environment; the prevention of physical and mental illness; the initial treatment of injury and sickness; and a medical liaison between the factory and outside medical services. It should aim at reducing the general sickness rate as well as the accident rate.'

DISEASE IN THE PRESENT WAR

Generally the chief diseases which engaged attention during the war of 1914–18 should be watched for and prevented by the same means in the present one. These means are the maintenance as far as possible of the normal health services; port sanitary control, purity of the water supplies; notification of infective diseases; hospital isolation; maintenance of adequate nutrition and so forth. Reference, however, may be made to certain diseases, which are the objects of our especial concern in the present war.

Deficiency diseases

Under the sure shield of the Royal Navy, the food supplies of Great Britain are being maintained, and the present scale of rationing is equitably administered by the Ministry of Food and is fully adequate for good nutrition. Scurvy, scurvy rickets, rickets and other deficiency diseases occur when high food prices prevail or when food supplies are restricted, inadequate nutrition also predisposes to the onset of acute and infective diseases. The prevention of such diseases is included in the economic defence of the country. Due provision is being made for milk for children and expectant mothers, and also for school meals for children and for communal feeding centres.

Tuberculosis

In 1938 all forms of tuberculosis were declining in Great Britain. The rate of decline in mortality had been greater since 1931 than at any other time during the present century. Progress has been retarded for the second time by the outbreak of a world war. War's baneful influence on tuberculosis mortality is already revealed by statistics. In 1939 the deaths from tuberculosis in England and Wales were 26,250 (war-time conditions prevailed only for a little over three months of that year); in 1940 the mortality was 28,144 and in 1941 it had risen to 28,669. Fortunately in 1942 the deaths from tuberculosis dropped to 25,500, a decline which has coincided with a lull in enemy bombing attacks on this country. The figures for the three complete war years do not include men and women in the Forces, but there is evidence to show a certain increase of the disease among them also. At the outbreak of war there was a temporary dislocation of the tuberculosis services in some areas, but excellent work is now being done, in spite of many difficulties. Evacuation, air-raids, shortage of nurses and of bed accommodation have all affected the normal service. The present

scale of rationing is regarded by experts as being adequate for tuberculous persons, if the diet is carefully planned, as it is in sanatoria and hospitals. Tuberculous milk is responsible for part of the increase in non-pulmonary tuberculosis, and universal heat-treatment of all milk is still to be desired. In war-time, contact infection, overcrowding and breaking down of bodily resistance to infection, through prolonged physical or mental strain, favour tuberculosis among persons in all callings. There has been an increase in mortality in mental hospitals and in mental deficiency institutions. Methods of prevention and treatment may be grouped into immediate and future measures. Miniature or indirect radiography is an important aid to early diagnosis, but it reinforces and does not supplant clinical examination. Recent work in chemotherapy encourages the hope that eventually a drug may be found which will destroy the tubercle bacillus in man (W. H. Tytler and A. D. Lapp, 1942; Annotation, *British Medical Journal*, 1942; News and Views, *Nature*, 1942.) After the war Great Britain will be faced with a greatly increased incidence of tuberculosis, particularly in ex-service men. More institutional provision and beds will be needed, and the village settlement and other means of rehabilitation will be required. The Ministry of Health is already taking steps to deal with this acute medical problem of war.

Venereal diseases

War-time circumstances, as is well known, favour the spread of venereal diseases. The general state of heightened nervous tension and excitement in persons lacking in self-control is one reason, and the transfer of large numbers of people, in military camps, in the neighbourhood of munition works or through evacuation to areas hitherto sparsely populated, may be associated with outbreaks of venereal disease in places unprovided with treatment centres. For such reasons the Ministry of Health has advised county and county borough councils in some districts to expand existing centres, and in others to set up new ones. With the reduction of transport facilities existing areas may not be able to serve such wide areas as formerly. As far as possible, specialist, medical and nursing staffs are to be retained, and to be expanded if necessary. The formation of mobile units has been suggested. During recent years medical knowledge has greatly advanced in the treatment of these diseases and much misery, social degradation, invalidity and crippling is preventable if the patient obtains early and skilled treatment. Chemotherapy may eventually prove to be as effective in preventing the spread of gonorrhoea as the arsphenamine compounds have been in syphilis. In 1942 the Minister of Health issued a regulation (Regulation 33B), which enables a medical officer of health to arrange on certain conditions for the compulsory treatment of persons known to be sources of infection.

Influenza

A close watch has to be kept on the figures of deaths from influenza. During the winters of the present war many cases of mild illness have occurred which have been ascribed to influenza, but so far there has not been any serious epidemic. It is presumed that there are other types of infection which may be clinically indistinguishable from that of the known influenza virus, and in which the aetiological agent remains unidentified. This makes the problem of prevention and treatment by influenza virus vaccine or serum more difficult.

Acute infective diseases

The importance of dealing promptly and efficiently with infective diseases has been emphasized already, and the measures adopted have been described. The movements of troops and of sections of the population, and the use of air-raid shelters provide increased opportunities for the spread of infection. As a war-time measure measles and whooping-cough have been made generally notifiable. Scabies, which had shown signs of increase prior to the war, continues to be prevalent and has demanded special attention.

Diphtheria.—This disease takes a heavy toll of child life, being the main cause of death among children between four and eleven years of age. Artificial immunization has greatly reduced the incidence of diphtheria in certain cities and districts in Canada and in the United States of America; such immunization is voluntary in Great Britain and in conjunction, therefore, with the treatment of patients in isolation hospitals, an active campaign has been in progress for some years to encourage immunization of the child population. This campaign has been waged with increased vigour by the

Ministry of Health since the war began, and prophylaxis is available free of cost. Much success has attended these efforts.

Enteric fever.—As in the war of 1914–18 the enteric group of fevers calls for special vigilance. Reliance for prevention rests chiefly upon supervision of the water supplies, upon general sanitation and upon detection of carriers. So far general immunization of the public has not been advocated, but the Ministry of Health has empowered local authorities to arrange for immunization of those desiring it in special circumstances, for example when an outbreak occurs. Aerial bombardments increase the risks of outbreaks of the disease by causing temporary failures in the efficiency of the sanitary services. Every precaution is being taken to protect these services throughout Great Britain and, when they are impaired, to put them back with all possible speed into a state of full efficiency.

Typhus fever.—The existence of louse-borne typhus fever in Europe and in north Africa at the present time makes it advisable to take precautions in case the disease reaches Great Britain through refugees, prisoners of war or returning travellers. A Memorandum (1941) on the subject has been issued by the Ministry of Health; it gives an account of the disease, of its diagnosis and of the measures of administrative control. It deals only with the louse-borne form of typhus fever, but points out that both the tick-borne and the flea-borne varieties have been introduced in the past to Great Britain. The following administrative measures are in force. (1) Notification to the medical officer of health, who must report immediately to the Ministry of Health. (2) Organization of teams in the principal towns for dealing with an outbreak. The teams comprise a medical officer, nurses, ambulance driver attendant, sanitary inspector and trained disinfectors. The staff members of the teams are provided with protective clothing and are offered preventive inoculation. (3) Expert consulting advice. (4) Hospital accommodation; disinfection arrangements.

Cerebrospinal fever.—Cerebrospinal fever is especially associated with war-time conditions. From the end of 1914 to 1918, cerebrospinal fever was epidemic on an unprecedented scale in Great Britain. Infection was widespread, but the majority of cases were notified in parts of England in which the largest numbers of troops were stationed. Before the present war the notifications of cerebrospinal fever had been rising, and in the years 1939 and 1940 there was a higher incidence of the disease. Fortunately the fatality rates remained low, that for 1940 being the lowest on record. Modern methods of treatment—particularly the use of sulphonamide preparations—have greatly reduced the number of deaths from this disease. The Ministry of Health has issued for the information of medical practitioners and medical officers of health a Memorandum giving information regarding the dose and use of sulphonamide preparations. In the prevention and detection of the disease full cooperation between military and civil sanitary authorities is all important. Fresh air, free ventilation in sleeping huts and billets, adequate inter-bed spacing and gargling with a simple disinfectant are desirable methods of prevention. Early clinical diagnosis and prompt treatment, without waiting for bacteriological confirmation, are essential.

CONCLUSION

It has been shown how vast a field is covered in Great Britain by public health organization and work in the present war. We have seen that totalitarian warfare affects the whole population of a country, that war slays its thousands but disease may slay its tens of thousands, and may seriously deplete the fighting resources of a nation; and that the maintenance of health concerns both military and civil populations, since disease and epidemics may spread from one to the other. It follows, therefore, that all measures directed towards the maintenance of national health and the prevention of disease bulk largely in the war effort of Great Britain. Fortunately also, in successive years of peace we have learned that the attack on disease is more than a question of doctor and patient. It comprehends a thousand matters of environment and social reform, in which many agencies play their part. All this complex organization is bent now towards health problems in a country at war, and our experience of cooperative effort is of considerable aid in this unprecedented work. The civil authority has the responsibility of hospital provision for civilians and for men of the Forces so far as they are not provided for by their own hospitals; it has organized a vast emergency medical and nursing service, and has coped with countless medical problems of the evacuation scheme. On the whole the civil arm is playing its part well in maintaining

the public health in the adverse conditions of war. The years of planning before the war have contributed much towards this fortunate result.

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SURGERY

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Each year cannot be expected to yield some outstanding surgical advance, nor indeed can it be certain, until perhaps long afterwards, that some new method which appeared promising on its first trial has really been an advance. In surgery new methods are often taken up so enthusiastically that they become almost a fashion; then as difficulties or disappointments begin to appear, there follows a period of neglect until on retrieval some of the methods either drop out or reach their proper level and eventually become part of current practice. But with very few exceptions each year that passes is signalized by great activity in surgical enquiry.

GENERAL SURGERY

Antiseptics

Penicillin.—At present there is great interest in the question of antiseptics and new preparations are being introduced with bewildering frequency. In *Medical Progress* (Critical Survey Section) 1943, penicillin was mentioned; high hopes are centred round this substance which shows such brilliant promise as a powerful weapon against the common forms of sepsis—even in their most devastating manifestations. This organic substance is difficult to manufacture and is at present available in only the smallest quantities, so that very properly it is being retained for carefully controlled trial by a few trained observers. The substance is bacteriostatic and not bactericidal at least in concentrations likely to be used therapeutically (M. E. Florey and H. W. Florey, 1943), so that while it prevents the multiplication of bacteria the body defences have the task of destroying them. In 1943 my Survey closed with a reference to that most deadly disease, septic cavernous sinus thrombosis, and the hope was expressed that it might be brought under control in the future. Now comes a report of a fulminating case in which recovery occurred after the use of penicillin (Florey and Florey). A varied selection of other trial cases also showed that many patients with generalized infections can be cured by the help of penicillin. The recovery of patients with apparently hopeless pyaemia and the healing in cases of acute osteitis without sequestrum formation are particularly striking. The most practical method of administration of this substance is by the intramuscular route at regular three-hourly intervals. Toxic symptoms have not been observed.

It was the enemy onslaught on the civil population by aerial warfare, with its holocaust of shocking injuries, that really prompted a renewed study of the problems of wound infection, and once again raised the questions: 'Can antiseptics prevent the growth of organisms in contaminated wounds?' and 'Is there any substance capable of ridding a wound of an established infection?'

Sulphonamides.—Sulphonamides can be used locally in a concentration which does not damage the living tissues and since they dissolve slowly they act as depot antiseptics. A certain optimum solubility has become a desirable property in antiseptics but since some act better against one organism than against another, the question arises of using combinations of the sulphonamides.

Flavines.—The flavines can control many infections without damaging tissues, and years ago George Crile showed that if it was necessary to interrupt an operation for toxic goitre for instance, the wound could be gently packed with gauze soaked in flavine and after forty-eight hours when reopened would be found without reaction. Dorothy S. Russell and M. A. Falconer (1941) showed experimentally that proflavine was innocuous to brain tissue. This substance can now be used as a crystalline powder and dusted into wounds, in this way overcoming the objection to flavine solutions which are largely taken up and held by the gauze (G. A. G. Mitchell and G. A. H. Buttle, 1942). This method of use is now on trial but it is too soon to conclude that it will prove ideal or even practicable.

Boric acid and potassium permanganate.—While the search for new and more potent remedies continues, efforts have also been made to discover means for more success-

fully employing older and well tried drugs that are both cheap and easily procurable. In this field it was found that a mixture of finely powdered boric acid and potassium permanganate, in a ratio of 100 to 1, was well tolerated on wound surfaces and did not damage the tissues. The powder dissolves in the body fluids and neither precipitates the protein nor impairs the cellular function, while it seems to encourage an outward flow of lymph and in that way facilitates drainage. This combination of remedies has been subjected to laboratory and clinical tests and is reported to be satisfactory (B. von Mezó, 1941; I. Györfy, 1941). It should be noted that experienced surgeons of all nationalities stress the point that chemotherapy does not replace but can only supplement the other and much more important measures for the treatment of wounds.

Prophylaxis of Peritonitis

The very extensive trial of antiseptics—using the word in an all-embracing sense has suggested chemotherapy as a prophylactic measure in abdominal conditions likely to give rise to peritonitis. This plan has been given a trial in the treatment of war wounds (S. Harild, 1942). A total of 10 grammes (150 grains) of sulphathiazole was distributed about the area of intestinal wounds and the neighbouring peritoneum; 2 grammes (30 grains) were used in the wound and 1 gramme (15 grains) was given by the mouth every six hours for from four to six days. The same plan is being given trial in civilians in the case of ruptured ulcer, of appendicitis and of other such conditions. So far the results are not convincing. In such conditions nothing makes so much difference to the results as early intervention. In injuries, whether they be military or civil, the importance of dealing most carefully with every possible source of infection, by searching out tiny holes and by protecting areas in which damage may lead to secondary necrosis, cannot be over-emphasized, for the most thorough and painstaking application of chemotherapy cannot compensate for surgical deficiencies. But there are late cases in which some additional safeguard would be most welcome and we want further experience to prove that the use of these substances does not do harm and to discover what is the best method of their application. Insufflators are on trial but as yet are not very satisfactory; dusting from a dredger or from a muslin bag must be limited to an exposed area and the crude substance left in bulk cannot be depended upon to diffuse widely while it dissolves. So there are practical problems and difficulties which demand attention and research. In this connexion it would be well to remember that though surgeons believed in the efficiency of irrigation of the peritoneum it was eventually proved that while it made little or no difference to the immediate results, secondary localized infections from diffusion were apt to occur subsequently.

The glove shortage

Another question related to antiseptics is the glove shortage, which threatens to become more acute. The first matter for consideration is the care and conservation of the available supplies of gloves. One way to lengthen the life of a glove is to use the same pair for several operations without removal from the hands. Between each operation the gloved hands are rinsed in plain water to remove blood and gross soiling, and are then thoroughly washed with household soap which is a better antiseptic than liquid or special soaps—indeed the absence of the latter need not be regretted. After this cleansing the gloved hands are immersed for five minutes in proved antiseptics such as 1 in 50 lysol or its affinities, or in 1 in 250 biniodide of mercury. It is hardly necessary to add that these very strong solutions are washed off in sterile water before the hands are allowed to touch the tissues. But the punctured glove is probably the greatest risk, and it has been shown that even with care 22 per cent of gloves are perforated at operations (L. A. Weed and Jessie L. Groves, 1942). If we reach the stage at which, with all the care and economies that can be devised, many operations must be done without gloves, then they should be reserved for the septic cases to help in carrying out the principle that the first duty of the surgeon is not so much to endeavour to clean his hands as to keep his hands clean! If those gloveless days arrive the surgeon must not 'dig for victory' and must avoid handling anything infected—as far as that may be consistent with the calls of his work. Before making rectal or vaginal examinations, the spaces beneath the nails and around the nail can be filled with softened soap and Vaseline freely used. It is essential to

keep the hands smooth and for this purpose glycerin or grease is most helpful but the former can hardly be obtained at present. What clean grease is available should be thoroughly rubbed into the hands at bedtime. For actual cleansing of the hands, thorough washing in hot water with household soap is certainly more important than the use of an antiseptic. For chemical substances to act they must be in contact for some time, so the hands must be soaked for as long as can be spared in the antiseptic solution selected. Beyond the importance of thorough washing it is unwise to be dictatorial about antiseptics, because what suits the skin of one individual may so irritate that of another as to set up roughness, and in that way may do as much harm as good. Those who were trained and who practised surgery before the use of rubber gloves became general, regard the possible shortage with much less misgiving than do others. (Halsted introduced rubber gloves for surgical purposes in 1890 but their use did not become general in this country until several years later.) We know that even with bare hands great care in technique can ensure excellent wound healing, but must admit that the uniformity of such results is much enhanced by the use of gloves.

Suture and ligature material

In some places there seems to be almost a crusade against the use of catgut, a material which has the enormous advantage that having done its work safely and completely, it harmlessly disappears. It is true that this material must be very carefully prepared and sterilized, and that up till now it has required shipping space and is consequently expensive. Further, it cannot be denied that catgut occasionally, although very rarely, harbours the spores of dangerous organisms also that in the process of absorption a certain amount of scar tissue forms. If an intestinal anastomosis or a wound disrupts catgut often gets the blame, but in most cases it is undeserved for there are many ways in which catgut can be misused (E. L. Howes, 1941). Nevertheless, considering the hundreds of miles of catgut which are buried in the tissues every year, the troubles for which it is really responsible must be very few indeed. Unabsorbable ligatures and sutures have grave disadvantages, and the memory of persistent sinuses and late inflammatory troubles which used to arise remains like a nightmare. Cotton thread can be used for most purposes and with the minimum of inconvenience attending unabsorbable material. It is cheap and easily sterilized and takes up little space. But the raw material should be handled as little as possible; it should be loosely wrapped in small quantities before sterilization and a fresh supply should often be prepared. Sterilization should be secured by boiling in a reliable antiseptic, such as 1 in 1,000 perchloride of mercury in watery solution, in which the thread can be safely stored for a week or two without deterioration.

Pulmonary embolism

Pulmonary embolism still remains a most tragic visitation in surgical cases, for it often carries off those patients who seem to be making the most favourable recoveries. Continued clinical and pathological studies confirm the original view that venous stasis and thrombosis are the underlying aetiological factors (T. H. Belt, 1939). Operative removal of such emboli has now been given a thorough trial, and the rare successes obtained by such an intervention have been dramatic and thrilling, but it can never be a practical method of dealing with the calamity, and surgeons are more and more driven to renewed study of suitable prophylactic measures. The work on heparin is still going on and must be looked upon as a continued experiment. Simpler methods are the avoidance of knee pillows and the regular use of bed exercises almost from the moment of recovery from the anaesthetic. Up-and-down movements of the legs several times during the day and deep-breathing exercises deliberately carried out for about fifteen times twice in twenty-four hours have been recommended, and have the virtue not only of simplicity but also of a certain measure of success (W. J. Potts, 1941). Another plan recommended is the division and ligation of the femoral vein in those cases in which the diagnosis of deep thrombosis in the limbs can be made. If this condition is bilateral, both femoral veins are ligatured (J. Fine and J. B. Sears, 1941). This plan may appear drastic but it is at least rational. If only observations can be made in some thousands of cases over a stated period of time, the value of these and other methods might be accurately assessed. What an opportunity is given here to great groups of large surgical hospitals like those controlled by the London County Council!

Peritoneoscopy

Endoscopic examination of the peritoneal cavity after inflation of air was first introduced to the notice of the profession about forty years ago by G. Kelling of Dresden. Considering the successes which have followed the extended use of other forms of endoscopy it seems rather remarkable that this particular plan has been so little used, at least in Great Britain. Just before the present war there was a revival of interest, but for the most part the work has been interrupted. There are reports that the method has been used in cases in which there is doubt whether or not some wound has actually penetrated the abdomen or has injured the bowel, and this question has been decided by peritoneoscopy (J. E. Hamilton, 1942). For the most part the method has been employed to settle the diagnosis when malignant disease has been suspected, or to determine whether or not there is such a degree of neoplastic extension as to render operation unsuccessful. But it would require a great deal more accumulated experience to convince most surgeons that in cases of real doubt the chance for or against some life-saving operation should be decided by this method of examination. It certainly has the advantage that the technique is extremely safe and that patients can leave hospital after twenty-four hours. New instruments tending to improve the technique have been introduced (Hamilton), and a considerable series of most interesting observations has recently been published (R. M. Walker and P. L. Playfair, 1942). Those who may be attracted by this method should bear in mind that it requires an experience of something like 200 cases before the appearances can be correctly interpreted.

Intramuscular injections

At a time when the intramuscular route is so much employed for the administration of medicaments as well as for saline and other infusions, it seems extraordinary that the buttock and to a lesser extent the deltoid regions are still regarded as the optimum sites. It might have been thought that the Trinidad case would have had some influence on the matter, to say nothing of the other cases recorded in which conditions like severe traumatic aneurysm have occurred after injection into the buttock (M. Paul, 1935). In 1920 I pointed out that the vastus externus muscle was admirably suited for such a purpose. This site presents a large mass of muscle well protected by strong fascia and without important vessels or nerves. Quite copious injections can be made without causing inconvenience and, if they must be continued, then both sides can be used, either one after another or alternately. The occasional inflammatory troubles and even abscesses which have occurred after injections are not dependent upon the site but upon the nature of the substance employed, but should such sequelae ensue there is no part of the muscular system in which they are likely to do less harm than the region of the outer aspect of the thigh.

WAR SURGERY

War wounds

Continued experience of war wounds has emphasized the extreme importance of the application of general surgical principles. The most important is the prevention of infection during the stage of contamination and before organisms begin to multiply in the tissues. It is very dangerous to assume that this period can be precisely defined in terms of so many hours, for it must depend partly on the virulence of the particular organism and partly on the susceptibility of the patient's tissues. It is a very wise plan to assume that the period of contamination passes into the period of infection after about six hours. This is not to say that an attempt at wound cleansing should not be made after the lapse of six hours, but to intervene within that period should be the aim of all surgical organizations. This largely reduces the problem to one of transport and this aspect is emphasized by nearly all the surgeons who have written about their experiences in the various theatres of military operations (H. von Haberer, 1942; E. G. Muir, 1943).

Surgical treatment.—When it comes to the details of the intervention required, it is recognized that the proper care of all but the clean through-and-through wounds probably demands a surgical operation with the patient under a general anaesthetic and under hospital conditions. It should always be remembered that such conditions can be improvised without the elaborate buildings and equipment which are usually associated with our hospitals in peace-time. It is generally necessary to enlarge wounds so that their depths may be properly explored; this enlargement has the

further advantage that it entails the free division of the deep fascia which is the great barrier against effective drainage. There is the further point that incision of the fascia allows of the consequent swelling of the muscles and other tissues, without the deleterious effects of severe tension. Some observers have drawn attention to the risk of a too free removal of the structures surrounding the immediate wound. Tissues torn and damaged beyond repair should certainly be cut away and as much of the muscle also as is necessary to expose healthy-looking and bleeding surfaces. But wide areas of skin should not be sacrificed and it is necessary to cut away only a margin of about a quarter of an inch from the wound edges. There should be great hesitation about the removal of fragments of bone. Any that are in contact with the original bone or are in the near vicinity should be left undisturbed, and only those fragments which are entirely free from periosteum and which lie in the soft tissues away from the parent bone need be taken away. When it comes to the question of closure the best rule is 'when in doubt leave the wound open'. All wounds would eventually heal if left open, but surgeons are naturally loth to give up the idea of closure by suture. To ensure that the depths of the wound are not sealed by the sides falling together, it may often be necessary to leave in lightly packed gauze, and drainage is facilitated if the gauze is well smeared with Vaseline. Plaster fixation is not only necessary for fractures but is also most effective in wounds limited to the soft parts, because it furnishes them with rest which seems so valuable in the prevention of absorption as well as in the promotion of healing (J. M. Barnes and J. Trueta, 1941).

Injuries to blood vessels

Another question that commonly concerns surgeons is the management of injuries of the great vessels. Should an attempt be made to suture arteries or is it better in the long run to depend upon division at the injured site with ligation of the ends? There is now enough experience to guide us in saying that it is necessary to consider repair of the vessel wall by suturing only in dealing with the common carotid, the common iliac and the popliteal arteries. If conservative measures can be employed with success in dealing with these vessels, they may prevent cerebral damage on the one hand or loss of limbs as a result of gangrene on the other. Stress is also laid on the great importance of preserving the blood supply. Without blood, tissues will not heal, and in the absence of a proper blood supply organisms are much more likely to multiply with disastrous effects. This brings us back to the old surgical aphorism attributed to one of the Gamgees : 'There is no antiseptic like life.' If tourniquets were completely debarred, probably less harm would be caused than by their indiscriminate use, but in this connexion it must be pointed out that firm packing of a wound to arrest haemorrhage may have just the same deleterious effect by cutting off the blood supply from the surrounding parts by the extreme pressure that may be necessary to arrest the flow of blood (R. Watson-Jones, 1943).

Nerve injuries

It seems to be agreed that in the difficult conditions of warfare it is better that nerves should not be sutured when the wound is first treated, but that they should be left for subsequent intervention when it can be assured that wound healing is complete and is without infection. Although this seems contrary to the ideals of reparative surgery it may be a matter of expediency and of great importance to the ultimate result. But there are several problems in connexion with delayed suturing. The first is whether or not something should be done to mark the nerve ends in order that they may be more readily found at a second intervention. For such a purpose it is suggested that if the ends are identified they should be fixed by a black silk stitch to the neighbouring muscle in the position in which they might be expected to be found if it were merely a question of retraction after division. It is now suggested that such an identifying suture should be left with long ends buried in the wound so that they may be more easily found. The next point concerns the effects of the sulphonamides. It has been found that these chemicals give rise to a degree of neuritis with positive anatomical changes which are harmful to the nerve and interfere with subsequent restoration of function. If this observation is substantiated, some other antiseptic must be used when nerves are divided. It must never be forgotten that the nutrition of the muscles and the movements of the joints must be carefully watched, so that these structures are ready to resume their function when the conductivity of the nerve is ultimately restored. In the later management of nerve injuries the question of nerve grafting still remains unsettled.

There has not been any uniformity of success even when autografts are used under ideal conditions, although there has been enough encouragement to stimulate continued experiment and enquiry. The uncertainty of grafting is embarrassing because the conditions for end-to-end repair are exacting. Apposition without the slightest tension appears to be essential and when there is an appreciable gap to bridge this is not always possible. The question of the effects of stretching nerves after suture has been very carefully investigated in connexion with the problem of those cases in which, to secure apposition, it has been necessary to flex joints fully (W. B. Highet and F. K. Sanders, 1943). It has been found that the process sets up degeneration and fibrotic changes in the nerves which interfere very much with subsequent complete recovery. Even when the conditions are ideal so far as apposition is concerned, the actual suture must be done with meticulous care. L. Guttman (1943) lays it down as essential that only epineural sutures should be employed and that as few as will suffice should be used. Catgut, because of the reaction attending its absorption, is not satisfactory, nor are pigmented silk or linen sutures. A trial has been made of human hair boiled for ten minutes and preserved in 70 per cent alcohol for twenty-four hours. From a practical point of view probably the finest of white silk is the most suitable of the available materials.

Foreign bodies

The proper management of foreign bodies is always a problem to those who have to embark on military surgery for the first time. In war surgery such foreign bodies are usually bullets, intact or fragmented, or portions of shell. It must also be remembered that very often there are secondary missiles consisting of portions of parts of equipment, clothing, bits of other weapons, pebbles and so forth. Such foreign bodies very often carry infection to the parts in which they lodge and they seem peculiarly apt to be a nidus for tetanus organisms. The natural history of foreign bodies in the tissues shows that sooner or later they tend to cause inflammatory mischief, to ulcerate into surrounding parts or to endeavour to find their way either outwards towards the skin or into the body cavities. During these processes they may give rise to much disturbance which may be of a very serious nature, especially when it occurs in the intracranial cavity or in connexion with the thoracic viscera. From a practical point of view there cannot be any doubt that on general principles such foreign bodies ought to be removed, but if that should be done at the time of the primary treatment of the wound or at a later date is a matter for the exercise of the surgeon's judgment. It is necessary to insist that all accessible foreign bodies should be removed at the time of the primary treatment of the wound. Although this practice may be accepted as an axiom when the limbs are concerned, it is extremely important to remember that more harm than good may be caused by attempts to extract foreign bodies say from the brain. When foreign bodies are healed in, they may be looked upon as in a quiescent state, and the question of their removal depends to a great extent on their size, their situation and the conditions associated with them. If their removal is going to mean a serious intervention then it seems expedient to advise that they should be left alone until they set up some active change, but at the same time it must be remembered that such changes may be deferred even for years. Sometimes the known presence of a foreign body sets up a train of psychological disturbances which may be an adequate reason for its removal. The tendency for foreign bodies to be associated with tetanus should be remembered in cases of late removal, so that the patient can be properly protected against an outburst of latent infection of this sort. A good deal is heard now about special probes and finders, but with an open wound it is well to remember that the finger is by far the best seeker (M. Kirschner, 1940).

Gunshot fractures of the jaws

Among all the belligerent nations it has been found necessary to pay special attention to these injuries, and this must be done at an early stage so as to provide the means of reasonable ultimate repair (R. Lehner, 1942). Basal anaesthesia is usually employed. It is most important that the bones or remaining fragments should be held in something like normal position, so that the difficulty of filling in gaps or of securing fixation will not be increased by the very gross displacement which is otherwise so apt to occur. An uninjured upper or lower jaw may be used as a splint for its fellow, but wire bridges between fragments or teeth will often be necessary. As free drainage as possible must be provided and sometimes this can be attained most successfully by

stitching back large flaps of the cheek. The tongue may have to be fixed temporarily to teeth or to cheek to prevent it from falling back and causing obstruction to the air entry. If tubes are used for drainage they should be carried down to the top of the sternum to conduct discharges well away from the wounds. Feeding problems are also difficult. It seems to be the rule to employ nasal catheters passed well down the pharynx and fixed into position. Probably temporary gastrostomy would be a great help in the management of some of these most difficult cases.

Phosphorus poisoning from lodging of exploding bullets

This is a new terror added to war injuries. A. J. Blaxland (1942) carefully records such a case in which an airman, who was wounded on 14th September, 1942 presented an entrance on the outside of the thigh with an abdominal injury which, at operation, was found to be a torn mesentery and jejunum. The remains of a ragged distorted German bullet were removed from the upper part of the mesentery. The injuries were successfully repaired and the patient responded well to the measures for treatment of shock. After making fair progress for three days the condition deteriorated and death occurred at the end of the sixth day. The necropsy disclosed extensive necrotic changes in the liver, with the histological features characteristic of phosphorus poisoning. It had been noticed that when the wound in the thigh was being dealt with it emitted a visible vapour with the smell characteristic of phosphorus. Examination of the bullet by an expert showed it to be identical with some bullets of an explosive type found on a wrecked German airplane. Each bullet contained three and a quarter grains of phosphorus, which is double the minimum lethal dose. The poisonous substance had been distributed among the tissues by the bursting of the bullet. It seems difficult to devise means of dealing with a situation of this sort and it raises speculation about what further horrors may yet be in store if similar methods of destruction are employed.

REGIONAL SURGERY

Gynaecomastia in men

Many cases are being observed among the large groups of young men which the armies of the world have brought under close medical supervision. The condition has been estimated to occur in about 1 in 4,000 men (J. M. Sullivan and R. A. Munslow, 1942). It is very commonly spoken about as being inflammatory in origin or due to some external trauma, and the story of the pressure of the trouser brace still seems to be accepted in one text-book after another. The condition occurs in otherwise apparently perfectly normal subjects. One breast may be enlarged, the enlargement of one breast may develop after similar enlargement of the other or much more rarely the condition may be bilateral. In unilateral cases the condition has sometimes been found associated with neoplastic or other lesions of the testicle (J. S. Richardson, 1943). As a rule no other disease is discovered and the condition usually gradually subsides quite independently of any treatment that may be employed. The conclusion seems to be inevitable that this abnormality is evidence of some endocrine disturbance of a passing nature. The practical point would appear to be that drastic treatment, such as excision of the breast, is very seldom called for. It would seem reasonable to treat any obvious departure from health such as a septic focus, severe constipation or anaemia. There is much to be said for the local use of a belladonna plaster which forms something of a protection and which at least deters the patient from manipulating the affected part. A similar condition may occur after the meridian of life is past and in such cases it is necessary to remember that malignant disease in the male breast does occur, although very rarely.

Non-specific epididymitis

Non-specific epididymitis is another of the conditions which occurs more commonly than was expected among the large numbers of young men undergoing active training. We must accept the fact that there cannot be any doubt that there are inflammatory conditions affecting the epididymis which are non-venereal and non-tuberculous. For long it has been known that such a condition may occur, although there has been a tendency to accept the patient's positive statement of a non-venereal causation very grudgingly. With many patients presenting themselves, this commonly repeated story has compelled attention. The condition may appear quite suddenly in otherwise healthy men; it is usually unilateral, and the manifestations include pain, swelling and a febrile upset. The one distinguishing feature about the local condition is the fact that

there is not any urethral discharge; the swelling is smooth and regular and abscess formation does not occur. By a process of elimination no signs will be discovered of the usual cause. As a rule, resolution occurs in from three to six weeks, but it may take longer and the patient may have relapses. Careful scrutiny of all the possibilities has established the probability that the condition is due to retrojection of urine along the vas, brought about by the unusual exertion of military activity. The likelihood of this explanation has suggested the wisdom of warning men about to undergo heavy physical training that they should empty the bladder as a preliminary. By way of treatment, rest, support and diathermy are probably the most helpful measures. Drugs do not appear to have any specific effect. Epididymis puncture may hasten resolution in indolent cases (Report, 1943).

Fractures of the hip

In old people these injuries are treated by a nail (Smith-Petersen) driven through the neck of the femur—a life-preserving measure which has saved an enormous amount of painful incapacity and lameness in many old people. There is still some discussion about the comparison of the results with the older methods and much controversy concerning points of technique, but there can be no question of the truly wonderful results that are attained in many of these patients, in comparison with the results that were usual before the introduction of the pinning method. It is perfectly marvellous to see these old people, many over seventy years of age, tripping about on their daily errands and with so little disability as to enable them to forget all about their accident. Occasionally the pins work loose and have to be removed and, of course, it would be ideal if the pin could be made of some absorbable material like, for instance, the deer's horn which has been employed in a few cases (E. W. H. Groves, 1939). Some careful reports on subsequent progress are now available, and A. L. Eyre-Brook and K. H. Pridie (1941) have reported in detail on seventy-five cases. Among them there were forty patients who were between sixty and ninety years of age, and the mortality of the whole series was only 5.3 per cent.

Diseases of the pancreas

The serum amylase test has proved very helpful in diagnosis, and is much more reliable than is the diastatic index or the mydriatic test. It is especially useful in acute types of pancreatic disease. The recognized normal is between 80 and 180 units, but readings of 2,000 and over are sometimes met with in pancreatitis (H. McCorkle and L. Goldman, 1942). The management of the haemorrhagic tendency by the proper use of vitamin K has opened up new possibilities for surgical intervention in malignant disease of the gland, and there are now several cases on record in which the head of the pancreas harbouring some malignant tumour has been successfully removed. But, quite apart from such radical surgery, much benefit has accrued in jaundiced patients because exploratory operation can be carried out with such a greatly lessened risk, and palliative measures such as anastomosis of the gall-bladder to some part of the gastro-intestinal canal can be employed much more freely than was usual in the immediate past.

Ulcerative colitis

In this troublesome disease some encouraging results have been obtained recently in desperate cases by terminal ileostomy, and dramatic recoveries have occurred. When the disease has lasted for months or sometimes for years, complete invalidism ensues and patients will willingly accept even a permanent external fistula if it is likely to bring relief. It was only in cases in which all other methods failed that this plan was first carried out, but the results have sometimes been so remarkable that many surgeons feel that an earlier resort to enterostomy is justified. Cases have been recorded in which the general condition has improved enormously and in one such case the patient doubled her weight in the first three months (R. Corbett, 1941). At first the intestinal fistula is a great nuisance, but after some few weeks the discharge becomes less liquid and after a few months is even semi-solid and, with a suitable apparatus, patients have been able to keep themselves perfectly comfortable and able to carry on their work in spite of what might have been expected to be a disabling procedure. Many surgeons have regretted the necessity for making such a fistula and have thought of it as being permissible only as a temporary measure, but when attempts have been made to restore the intestinal canal the intervention has been attended by a very considerable mortality, and even in those cases in which the bowel has been success-

fully restored there has often been a recurrence of the trouble in the colon. If there is direct symptomatic evidence of continued disease confirmed through the sigmoidoscope and by opaque enema and so forth, it is possible that a partial colectomy might be a second stage and that at a third intervention the canal might be restored, the small intestine being implanted in a part of the colon which has completely recovered. A review of the whole problem opens up a vista of hopeful possibilities and work should undoubtedly continue along these lines.

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OBSTETRICS AND GYNAECOLOGY

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OBSTETRICS

Maternal nutrition and maternal and foetal morbidity and mortality

There has been considerable work done on these subjects within the past few years; this is conveniently considered under the following headings.

The mother

Anaemia.—R. A. McCance and E. M. Widdowson (1942) suggested that the national 85 per cent extraction flour may, because of its phytic acid content, lead to a reduction in the absorption of iron and calcium in the body. There is some evidence that deficiency anaemia is on the increase among women and infants (Lucy Wills, Helen M. M. Mackay, Kaitilin Bingham and R. H. Dobbs, 1942). H. A. Hamilton and Helen P. Wright (1942) examined 392 pregnant women from the third month onwards. Half of this number with an average initial haemoglobin level (Haldane) of 75 per cent were given iron; the remainder had an average initial level of 79 per cent. At the end of pregnancy the respective haemoglobin levels were 77 and 70 per cent. The above authors conclude that women of the working class are more anaemic than they were before the war.

Calcium and vitamins A, B, C, D—There is not at present any evidence in regard to calcium shortage in pregnant and nursing women and in infants. It is stated that the intakes of vitamins A and D are relatively satisfactory in the British Isles, because of the priority in milk for mothers and infants and because of the fortification of margarine. The substitution of 85 per cent extraction flour for white bread has improved the situation in regard to the B complex. There is, however, some evidence of shortage in vitamin C (L. Harris, 1942), and there is a general belief that a vitamin C supplement (from 50 to 100 milligrams) should be given to expectant and nursing mothers.

Toxaemia.—K. Utheim-Toverud (1939) claimed that by ensuring an ample diet for pregnant women, the incidence of this disease was reduced. In 312 women who had not had any special care the incidence was 1·6 per cent, whereas in 105 women with a reinforced diet the incidence was nil. The People's League of Health investigation on 5,000 women in ten London hospitals (1942) gave similar results. To 2,500 pregnant women supplementary minerals (iron, calcium, iodine, manganese and copper) and vitamins (A, B complex, C and D) were added to the diet. In the primiparae the incidence of albuminuric toxaemia in the controls was 7·4 per cent, as compared with 5·4 per cent in the treated women. In the multigravidae the relative percentage incidences were 5·2 and 3·6. It should be noted that the sepsis rate was similar in the control and in the treated groups.

The infant

Abortion, prematurity and still-birth.—Utheim-Toverud found that in a home for unmarried mothers the prematurity rate in 223 women who resided in the home was 3·1 per cent, as compared with a rate of 27·2 per cent in 125 women who were admitted just before delivery. The percentage frequency of infants below 5½ pounds (immaturity) was 2·2 in the former and 16·0 in the latter. In another group of 105 women who had special antenatal supervision, including the administration of cod-liver oil and iron in cases of anaemia, the prematurity rate was 1·9 per cent. In an untreated control group of 312 the rate was 6·0 per cent. J. H. Ebbs, F. F. Tisdall and W. A. Scott (1941) gave adequate food supplements to 90 women of poor social status. In them the still-birth rate was nil, and the abortion and prematurity rate was 2·2 per cent. In a control series of 120 pregnant women of the same income group who did not receive any supplements, the still-birth rate was 2·2 per cent and the abortion and prematurity rate 14 per cent. In the People's League of Health investigation (1942) the prematurity rates were as follows: primiparae, treated, 20 per cent, controls 23·9 per cent; multiparae, treated, 20·1 per cent, controls 24·2 per cent. D. Baird (1942)

has shown that the prematurity rate is influenced by the income level. Thus amongst booked hospital cases, he found that the rate was 23 per cent, whereas in private practice it was 8 per cent. He states further (1943) that the still-birth and neonatal death rates were higher in hospital practice—3·3 as against 0·6 per cent in private cases.

Haemoglobin levels and puerperal morbidity

H. J. Bickerstaff (1942) points to the well-established fact that there is a relation between the incidence of puerperal infection and the amount of blood loss at delivery. This observation led him to investigate the question and, in addition, to discover how far the haemoglobin level before delivery is related to puerperal morbidity. Haemoglobin determinations within four weeks of delivery were available in 1,001 cases. He found that, with increasing haemoglobin values, the rate of morbidity decreased and that this relationship persists through and above a haemoglobin range ordinarily considered satisfactory. He found the same relationship in regard to blood loss at delivery; 2,015 such cases were investigated. With losses of 600 cubic centimetres or more, fever rates were from two to ten times the rates for lesser amounts of bleeding. Blood loss within 'normal' ranges was not demonstrably related to febrility; in such women the prenatal haemoglobin level is a determining factor.

Simplified diagnostic tests for pregnancy

U. J. Salmon, S. H. Geist, A. A. Salmon and I. L. Frank (1942) claim that urinary prolan causes a distinctive hyperaemia of the ovaries of the immature rat six hours after injection. They injected three animals weighing between thirty-five and forty grammes with 2 cubic centimetres of morning urine and carried out necropsy after six hours. The result was positive in seventy-seven out of seventy-eight tests with pregnancy urine, and was negative in all of thirty-five with non-pregnancy urine. S. Aschheim (1942) injected 0·5 cubic centimetres of the urine subcutaneously into two immature rats, from four to five weeks old, and vaginal smears were made at the end of seventy-two, eighty-four and ninety-six hours. With pregnancy urine, only epithelial cells were found at seventy-two hours and after from eighty-four to ninety-six hours, keratinized cells. The keratinized cells constitute the criterion of a positive reaction. The animals can be used repeatedly.

Effect of ergot in promoting involution of the post-partum uterus

C. Moir and C. S. Russell (1943) report controlled clinical experiments involving two series of cases, the first totalling 589, the second 78. The observations did not give any support to the common belief that ergot administered over a period of days in the puerperium hastens involution of the uterus. In a theoretical discussion, the authors point to the well attested facts that the hypertrophy of the uterus during pregnancy and the rapid diminution during the puerperium are mainly governed by the level of oestrogenic hormone in the blood stream. They suggest that an unimpeded blood supply will favour involution and that ergot administration, by causing unnatural spasm of the muscle, will tend to slow the process. Under natural conditions the puerperal uterus shows increasingly prolonged periods of relaxation which favours the blood flow; this natural process is apt to be disturbed by ergot and this may in its turn interfere with the involution process. The authors maintain that vast quantities of the drug are daily used for purposes that may be fairly described as wasteful, useless and possibly even harmful. During the war importation of ergot is difficult and uncertain.

Hormonal influences on the ureter during pregnancy

J. M. Hundley, Jun., W. K. Diehl and E. S. Diggs (1942) studied this question in 130 normal pregnant women. During the early part of the first trimester the peristaltic behaviour of the ureter was nearly similar to that occurring in the non-pregnant woman. As pregnancy advanced there was a continued and gradual decrease in the frequency as well as in the amplitude of the contraction waves, until in the seventh and eighth months a complete atonia existed. This atonia continued up to a short time before delivery. There was then a return of the same peristaltic activity as was seen during the latter part of the first trimester. By means of a hydrophorograph, a closed system in which the urine from a ureteral catheter passes beneath a tambour, the variations of urinary pressure were recorded on a moving graph. Tracings in normal

pregnant women who received stilboestrol showed considerable activation of ureteral peristalsis, whereas positive decrease in contractions was produced by progesterone.

The mechanism and treatment of occipitoposterior position

D. A. D'Esopo (1941) considers that this position is determined mainly by narrowing of the forepelvis in the presence of an ample anteroposterior diameter. The majority (70 per cent) of such cases are capable of spontaneous delivery but, at the same time, the condition is responsible for more dystocia than the other vertex positions. The pelvic architecture shows marked variations and the types of rotation vary accordingly. Two special forms of architecture are found especially in posterior positions, namely those in which the transverse diameters are contracted at the brim or the midpelvis or at both levels with compensatory increase in the anteroposterior diameter and, conversely, those in which the anteroposterior diameter is shortened because of a flat posterior segment at the brim or a projecting sacrum in the midpelvis whilst the transverse diameters are ample. The varying mechanisms involve different treatments. When there is arrest of rotation due to a narrow anthropoid brim, the head is pushed up and rotated above the brim, or version is carried out. When arrest is due to narrow spines in android types, the head is pushed up and rotated above the spines or above the brim, or version is carried out. When the posterior aspect of the brim is flat, rotation is carried to the transverse only and, in this position, the head is brought into the lower forepelvis, thereby converting it into a deep transverse and rotation is then carried out. If in such cases deep transverse arrest has occurred the same rotation procedure is carried out. When the head is arrested in a direct occipitoposterior position delivery without rotation should be carried out only if the sacrum is not encroaching; in most cases the head should be rotated. When the head is low and is well moulded and well flexed, manual rotation is the desirable procedure. Rotation at the level of arrest is rarely a procedure of choice, because in most cases there is some obstruction preventing rotation at that level. For this reason the Scanzoni manoeuvre involving simultaneous traction and rotation is undesirable with a well moulded and well flexed head.

The eclamptic phenomenon and placental ischaemia

J. Young (1942¹) claims that a study of the placental lesion found in eclampsia and in the pre-eclamptic toxæmia of accidental haemorrhage helps to throw light on some questions of aetiology. The degree of the toxæmia is determined by two related factors: (1) the extent of the ischaemic lesion in the placenta and (2) whether or not the foetus survives this lesion, or in other words, whether or not the circulation is maintained in the undamaged portion of the placenta. If the lesion is sufficiently massive to cause immediate death of the foetus and immediate and complete cessation of circulation in, or birth of, the placenta as occurs in many (75 per cent) cases of accidental haemorrhage, there is no toxæmia. If however the lesion, whilst still considerable, is compatible with foetal survival for some hours (25 per cent), toxæmia occurs. Young refers to the analogy between the toxæmia which occurs after crushing air-raid trauma of tissue and the toxæmia due to placental ischaemia. In a later paper Young (1942²) adduces further evidence in support of this analogy. In four fatal cases of accidental haemorrhage a renal lesion similar to that found in cases of fatal anuria coming on after the crush syndrome (E. G. L. Bywaters and D. Beall, 1941) was present. This lesion consists of tubular degeneration involving especially the ascending limb of Henle and the second convoluted tubules, with the deposition in the tubules of haematin casts. Young points to the fact that this analogy includes the eclamptic phenomenon in general, since it has long been known, from the work of Fahr and others, that fatal cases of eclampsia commonly exhibit a similar tubular lesion in the kidneys with haematogenous casts. F. F. Snyder (1942) has produced accidental haemorrhage (premature separation of the placenta) experimentally in pregnant rabbits by injection of urinary prolactin. This induces an aberrant ovulation which leads secondarily to 'utero-placental apoplexy'. In view of Young's work it is interesting to find that a number of Snyder's animals died of general toxæmia; necropsy showed massive necrosis of the liver and degenerative lesions in the kidneys.

Syphilis in obstetrics

S. J. Benenson (1942) reports an investigation on 935 syphilitic pregnant women. In 789 women who were treated 93.3 per cent of the children were saved, whereas in

146 untreated women only 61 per cent gave birth to apparently non-syphilitic infants. Benensohn advised that all women with a history of syphilis should be treated during each pregnancy irrespective of the amount of previous treatment or serological reactions.

Serological tests.—E. D. Plass and Naomi Sacks (1942), between 1926 and 1938, found syphilis or a strong reason for suspicion of syphilis in 400 out of about 11,000 pregnant women, that is 3·6 per cent. None of the methods employed for the detection of syphilis in the new-born infant, namely serological investigation of cord blood or venous blood, examination of the placenta and X-ray examination of the long bones, has been found reliable. The above workers believe, however, that serological tests at the age of two or three months are reliable. It is of interest to note that one out of the eleven children of congenitally syphilitic mothers had syphilis. They refer to the occasional unreliability of a negative serological finding in the mother; the infants of two such mothers were syphilitic. Their uncorrected foetal salvage was 85·2 per cent and, if fourteen abortions are excluded, 88·5 per cent. Four of the 254 women treated by Plass and Sacks in hospital died from arsenical encephalitis and altogether there were reactions in 12·2 per cent.

Arsenical encephalitis.—R. E. Arnell and W. F. Guerriero (1942) report two fatal cases of arsenical encephalitis occurring after the administration of neoarsphenamine to pregnant women. In the hospital in which they work the mortality rate from arsenical encephalitis in pregnant women was 0·76 per 1,000 injections, a figure four times greater than the rate in non-pregnant women of the same age group. In each case here reported the fatal issue occurred after relatively small dosage, in one after 0·9 gramme had been given by two injections in seven days. The intolerance in each case first appeared after the last injection and was expressed as headache and mental confusion, and subsequently by muscular spasms, coma and death. The authors state that there is increasing evidence that pregnant women are more susceptible to these reactions and that the risk is greatest when the treatment is started late in pregnancy. R. B. Nelson, C. McGibbon and F. Glyn-Hughes (1943) report three further cases during pregnancy.

Sulphanilamide powder in obstetric and gynaecological operations

Within recent years sulphanilamide powder has been used extensively for the control of external forms of sepsis in wounds, throat infections and other similar conditions. J. D. Bibb (1942) discusses its use in obstetrical and gynaecological operations. The indications for its use in the presence of active infection are peritonitis and abscess cavities which have been opened, for example in the pelvis or in Bartholin's gland. The prophylactic uses are after or when there is a risk of contamination of the peritoneal cavity, for example in pyosalpinx, and for the prevention of adhesions. In the prophylaxis of peritonitis eight grammes (120 grains) are used. Before use the powder is treated in tubes at 140° C. in a dry oven for two hours. It should be thinly and evenly spread. After such local application it is undesirable to give more by oral administration for three days afterwards. C. T. Beecham and R. Friday (1942) state that sulphanilamide powder causes necrosis of fatty tissue and that it should not be placed in wounds.

Rupture of splenic and renal aneurysms during pregnancy

R. A. Lennie and H. L. Sheehan (1942) report two cases of rupture of an aneurysm of the renal artery which occurred over a course of ten years in the Glasgow Maternity Hospital. A review of the recorded cases shows that splenic aneurysm generally occurs in young adult women, whereas renal aneurysms are more common in young adult men. If a woman in the later stages of pregnancy develops sudden upper abdominal pain and is found to have much free blood in the peritoneal cavity, which is not due to an obstetric complication, the possibility of a ruptured aneurysm must be borne in mind. A large haematoma in the kidney region should suggest a ruptured renal aneurysm. The only successful method of dealing with such catastrophes is rapid recognition and heroic surgery. The affected artery must be ligated proximally to the aneurysm and, if possible, the spleen or the kidney should be removed.

GYNAECOLOGY

Methods for determining the time of ovulation

J. Rock (1941) reviews the literature on the subject and reports his own findings.

Mittelschmerz.—Some women have a momentary lancinating pain in one or other iliac fossa each month at the time of ovulation. In my opinion, however, it cannot always be assumed that *mittelschmerz*, which is an important clinical entity, in most cases associated with a free leucorrhoeal or blood-stained discharge at the time of the pain, is directly determined by ovulation, for in some cases the recurring monthly pain is always on the same side (Young).

Intermenstrual bleeding.—G. N. Papanicolaou reported that about 24 per cent of vaginal smears taken on the fourteenth day of the cycle contained microscopic blood; in less than 5 per cent of women this blood is recognized clinically.

Biochemical assays.—Assays of the oestrogens in blood and urine may be informative.

Basal body temperature.—B. B. Rubinstein has described a specific rise in the rectal temperature at the time of ovulation, but Rock does not believe that this observation is reliable.

Vaginal smears.—The cyclical changes in the human vagina are less reliable than those occurring in the lower animals, in which oestrus (and ovulation) is associated with marked desquamation.

Biopotentials.—In 1935 H. S. Burr and his collaborators claimed that in rabbits there was a demonstrable increase in the difference in potential between two electrodes, one placed over the symphysis, the other in the vagina. This method is unreliable in the human subject.

Endometrial biopsy.—This is the best clinical test for ovulation. In about 10 per cent of 392 infertile women Rock found evidence of anovulatory menstruation.

Sterility due to absence of ovulation

L. S. Griffith and W. P. L. McBride (1942), by means of premenstrual endometrial biopsy, found evidence pointing to absence of ovulation in sixteen of forty-two sterile patients. They quote the incidence of anovulatory cycles in sterile women as given by different observers: C. Mazer and S. Israel, 33 per cent, S. L. Siegler, 29 per cent; E. Novak, 48 per cent. J. Rock, M. Bartlett and D. Matson found that 9 per cent of 392 sterile women had an occasional anovulatory cycle, and 4 per cent a habitually anovulatory cycle. The writers found evidence of ovulation after the use of pregnant mare's serum in seven of eight anovulatory cases. In one patient pregnancy occurred and this ended in abortion.

Endocrine treatment

The use of oestrogens in spasmodic dysmenorrhoea.—For many years I have used oestrin preparations with advantage in the treatment of spasmodic dysmenorrhoea. In a large proportion of cases the relief is considerable or complete so long as the therapy is continued each month, but relapse is usual after cessation of treatment. I have generally employed moderate daily doses (10,000 international units) for ten days before the expected period; latterly I have used from 0.5 to 1.0 milligram of stilboestrol for the daily dose. The benefit has been theoretically ascribed to the temporary activation of the hypofunctional uterus which is generally present in such cases. S. H. Sturgis and J. V. Meigs (1942) use 10 milligrams of oestradiol dipropionate injected six days after the onset of menstruation and repeated three times at ten-day intervals. The treatment effects only a temporary relief. It is given for three months, and one month is allowed to lapse before the treatment is continued. It does not lead to a permanent cure. The authors believe that the oestrogen operates by suppressing the action of the anterior lobe of the pituitary gland and thus inhibiting ovulation.

Stilboestrol in functional uterine haemorrhage.—W. K. Cuyler, E. C. Hamblen and C. D. Davis (1942) found that, in fifteen women who had prolonged and excessive uterine bleeding, the oral administration of diethylstilboestrol in a daily dosage ranging from 6 to 2 milligrams produced arrest of the bleeding in eleven patients in from two to eleven days, the average being 4.4 days. The writers found that 6 milligrams was the most effective dose, the arrest occurring in from two to five days, with an average of 3.3 days. Smaller doses caused arrest of the bleeding but required a longer time to produce this result.

Prevention of nausea and vomiting in stilboestrol therapy.—R. R. Greene and E. M. Dorr (1941) studied the correlation between the dose and the incidence of nausea and vomiting after oral administration of stilboestrol in 127 patients and after parenteral administration of stilboestrol dipropionate. Reactions were more common with the larger doses. Dorr starts oral treatment with stilboestrol by giving a dose of 0.1

milligram daily, increased after one or usually two weeks to 0.2 milligram if there is not any improvement. After each interval (of one or two weeks as the case may be) the dose is raised to 0.5, 1, 1.5 and 2 milligrams as necessary until the patient is relieved of the symptoms. This procedure may entail a lapse of a fairly long interval before the symptoms are relieved, but only 22.5 per cent of patients needed doses larger than 0.5 milligram. With this graduated dosage none of the patients suffered undesirable reactions.

Implantation of oestrogens for menopausal symptoms.—U. J. Salmon, S. H. Geist and R. I. Walter (1941), in a study of 180 women, found that in the case of α -oestradiol and α -oestradiol benzoate the implantation of loose crystals is more effective than that of compressed tablets. They found that crystals or pellets were more effective than the same materials dissolved in oil. Subcutaneous implantation of loose crystals of α -oestradiol in amounts of from 10 to 25 milligrams is a simple, safe and effective method for ordinary menopausal symptoms, and for those appearing after surgical or X-ray sterilization. They also recommend it as a prophylactic measure at the time of bilateral oophorectomy. H. G. Bennett, Jun. and R. W. Te Linde (1942) found the implantation of pellets of crystalline oestrone satisfactory in 93.4 per cent of cases. The benefit is more lasting than that of any other method, and the pellets did not produce any of the untoward side-effects found sometimes with stilboestrol or with oestradiol preparations. The authors did not find vaginal smears to correspond to the degree of clinical change.

Androgens in gynaecology.—S. H. Geist and U. J. Salmon (1941) treated 422 women by means of androgens over a period of five years. If used in doses not exceeding 300 milligrams a month androgens do not cause masculinization effects, namely deepening of the voice and slight enlargement of the clitoris. The writers found androgen preparations of value in functional bleeding, in functional dysmenorrhoea, in premenstrual mastopathies, in post-partum engorgement of the breasts and in certain types of the menopausal syndrome. Methyl testosterone is effective when given by mouth.

Fibromyoma of the uterus

Experimental production of fibromyoma.—A. Lipschutz (1942) has produced subperitoneal uterine fibroid tumours in guinea-pigs by subjecting them to prolonged treatment by oestrogens. The work confirms the previous findings of W. O. Nelson (1937). Lipschutz has also found that the experiment led to the development of fibromyomas in the mesentery, spleen, pancreas and abdominal wall. All types of oestrogens were effective and for the induction of tumours continuous administration is essential. When the oestrogens were combined with progesterone or with testosterone the fibromatogenic effect was inhibited. R. Marx, S. Glass and A. Shulman (1942) have repeated the experiments with similar results.

Myomectomy.—H. E. Miller (1942) believes that myomectomy should not be carried out except by an experienced gynaecologist. The ideal age for the operation is between twenty-five and thirty-eight years. With proper limitations it is applicable to about 10 to 15 per cent of all cases of uterine fibromyoma seen in private practice. Recurrence of the tumours occurs in about 3 per cent. Symptomatic relief in regard to menstrual excess and dysmenorrhoea can be looked for in 80 per cent. Myomectomy should not be performed for sterility until other factors have been carefully considered. The reported successes have been as high as 33.3 per cent. I. C. Rubin (1942) states that before undertaking myomectomy the surgeon should exclude the existence of retained placental fragments, submucous myoma, polypi and carcinoma. Practically all intra-uterine lesions can be demonstrated by means of radiography after the injection of a radio-opaque medium. If the operation is devised for sterility, care should be taken that the uterine ends of the tubes are not compromised by the incision. Recurrence was rare and pregnancy has subsequently occurred in from 25 to 35 per cent of cases.

Leucoplakia, kraurosis and senile vaginitis

C. L. Buxton (1942), in twenty-one patients suffering from these conditions, used a lanolin ointment containing diethylstilboestrol. Amounts containing 10 milligrams of the oestrogen were applied locally each day for a week. If improvement occurred it was usually apparent within one week but in unimproved cases the treatment was tried for one month. Of nine patients with senile vaginitis and kraurosis, five were completely relieved, one was improved and two were unrelieved. In seven cases of leucoplakia two patients were completely relieved, one was improved and four were

unrelieved. Three out of sixteen women remained symptom-free after one month's treatment; thirteen required to continue using the ointment once or twice weekly to prevent recurrence of symptoms. Several patients obtained relief from accompanying hot flushes and had uterine bleeding after cessation of treatment.

Gonorrhoea

Sulphonamide treatment of gonorrhoea in the female.—R. G. Douglas, Iona F. Davis and J. F. Shandorf (1942) investigated 158 women with proved gonorrhoea admitted to the New York Lying-in Hospital. With adequate exposure of the vulva under good light the labia are held far apart, bringing the external urethral meatus into view. The area just within the meatus is first cleaned with a sterile applicator which is then discarded. The urethra is massaged from back forward and from each side to the midline. The exudate thus expressed is collected on a small moist sterile swab. Smears are prepared, and after reapplying the swab to the urethra it is plated directly on a chocolate agar plate. Cervical exudate for similar studies is obtained from the endocervix after cleaning the vaginal vault with a sterile cotton ball. The authors believe cultures to be more reliable than smears for diagnosis and for control of treatment. The latent form of the disease is often asymptomatic or is associated with leucorrhoea only (43 per cent) and very commonly cannot be recognized without culture. The treatment is more efficient if the patient is admitted to hospital as an in-patient. The authors used sulphanilamide (sixty-four cases), sulphathiazole (sixty-two cases) and sulphadiazine (fifty-nine cases). They found that the two last preparations were more specific and more rapid in their action and were considerably less toxic. Sulphadiazine appears to be slightly more efficient than is sulphathiazole, and is the least toxic. Bacteriological 'cure' is generally obtained within from nine to ten hours after sulphathiazine administration, and from forty to fifty hours after the giving of sulphanilamide. Four grammes (60 grains) of sulphadiazine or sulphathiazole in divided daily doses for six consecutive days constitutes, at the present time, the ideal form of therapy. Bacteriological 'cures' were established in 180 out of 185 admissions of 158 female patients. There were twenty-seven recurrences, which were thought, for the most part, to be new infections. There were four failures with sulphanilamide and one with sulphadiazine.

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ALIMENTARY TRACT DISEASES

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HYPERTROPHIC GASTRITIS

Diagnosis

Every experienced sigmoidoscopist is aware of the remarkable change in the appearance of the rectal mucosa produced by spasm. The thin pink mucosa of the fully relaxed rectum with its blood vessels clearly visible suddenly becomes dark red and congested, and so thick that it may completely obliterate the already narrowed lumen. If slight proctitis is present innumerable minute bleeding points appear, although none was visible in the relaxed rectum. If spasm is present throughout the examination an erroneous diagnosis of hypertrophic proctitis might be made by the inexperienced, and when the rectum is relaxed to an unusual degree the mucous membrane appears so thin and pale that it might be regarded as atrophic. The contrast, however, is quite natural because the thickness of the mucous membrane must vary inversely with the diameter of the rectum at the moment of observation.

From analogy with the changes in the normal rectal mucosa, it might be expected that appearances resembling that of hypertrophic gastritis and of atrophic gastritis would be closely simulated when the muscular coat of the part of the stomach involved is in a state of contraction and of extreme relaxation respectively. That this is true is proved by the observations of H. A. Magnus and H. W. Rodgers (1938) who found by biopsy and by post-mortem examination of the mucous membrane of stomachs previously observed by gastroscopy, that in most cases diagnosed as hypertrophic gastritis no hypertrophy was actually present. Here then is the explanation of the remarkable difference in the incidence of hypertrophic gastritis as recorded by various observers. There is no doubt that an inexperienced gastroscopist, or one who has not had any opportunity of comparing his gastroscopic findings with biopsy or with necropsy specimens, often diagnoses hypertrophic gastritis when he sees a normal mucous membrane which is at the moment thickened owing to contraction of the wall of the stomach. H. L. Tidy (1943¹), H. C. Edwards (1943) and J. F. Venables (1943) have recently emphasized the danger of converting a mild functional dyspepsia into a severe gastric neurosis by lowering the medical category of the patient because of an erroneous gastroscopic diagnosis of hypertrophic gastritis. I have no doubt that this is a common occurrence both in the Army and in civil practice, since only a small proportion of those now practising gastroscopy are capable of interpreting what they see. Thus A. M. Gill (1943) diagnosed hypertrophic gastritis in no fewer than 166 out of 806 soldiers admitted for chronic dyspepsia whom he gastroscopied, compared with forty-three with gastric ulcer, whereas Edwards, a pioneer of gastroscopy in England, found only five cases among eighty-six soldiers selected for gastroscopy out of 346 patients in whom radiological evidence of disease was in doubt or was negative, but all of whom would presumably have been gastroscopied by Gill, so that an incidence of 1.4 per cent in Edwards's cases is comparable with Gill's 20 per cent. Uncomplicated hypertrophic gastritis is in fact rare compared with gastric ulcer at all ages, and especially in the young. It is very resistant to treatment although, in my experience, lavage every morning with 1 or 2 per 1,000 silver nitrate when the patient is fasting, together with an unirritating diet, eventually leads to recovery in the majority of cases. If left untreated hypertrophic gastritis is a serious condition because the hypertrophied mucous membrane may eventually undergo malignant change.

THE EFFECT OF EMOTIONS ON THE STOMACH

Clinical observations

S. Wolf and H. G. Wolff (1942) have carried out some remarkable observations on the effect of spontaneous emotional disturbances in a patient with a large gastric fistula, the mucous membrane of which was exposed to view. When the man was apparently contented the mucous membrane was pink and continuously secreted a small quantity of gastric juice containing free hydrochloric acid; small rhythmic contractions also occurred. Beef broth introduced through the stoma led to increased

acid secretion with hyperaemia and vigorous contractions of the stomach wall. Fear and sadness were accompanied by pallor and by inhibition of secretory and of motor activity, whereas anxiety, hostility and resentment were accompanied by increased secretion of acid with hyperaemia and hypermotility associated with heart-burn and abdominal pain. The appearance of the thick hyperaemic mucosa resembled that described by gastroscopists as hypertrophic gastritis, and the frequency with which this diagnosis is made by some observers is probably due to the temporary changes induced by the patient's fear of the examination being mistaken for organic disease. Intense anxiety for a period of a fortnight gave rise to severe and prolonged hypersecretion, engorgement and hypermotility, and bleeding-points frequently appeared. In this state the most trivial injury caused by stroking with dry gauze or striking with a glass rod gave rise to haemorrhagic erosions, which were quickly covered by mucus and healed within twenty-four hours. If, however, the protective mucus was continually brushed away and the erosions were kept constantly exposed to gastric juice, a chronic ulcer developed. These observations throw a new light on the influence of emotions in the production of peptic ulcers.

DENTAL DEFICIENCY AND GASTRIC DISORDERS

Pyorrhoea and apical infection

In the past it has been usual to regard pyorrhoea alveolaris as the main dental cause of gastric disorders. The acid gastric juice, however, rapidly destroys the streptococci swallowed from the mouth, and living bacteria can rarely be isolated from the gastric contents except in the presence of achlorhydria (F. A. Knott, 1923). Even with the latter there is not any evidence that the intact gastric mucosa is ever invaded by streptococci from the lumen of the stomach. The part played by pyorrhoea in the production of gastric disorders has in fact been much exaggerated. The work of E. C. Rosenow (1916, 1923), which appeared to show that apical dental infection is an important factor in the production of peptic ulcer, has not received any confirmation and is now generally discredited. There is thus no justification for the extensive extractions for pyorrhoea and apical infection which are so often carried out as treatment for dyspepsia.

Gastric carcinoma in edentulous patients

In contrast with the negligible part played by dental infection in the production of gastric disorders, a deficient masticatory surface is probably of great importance. The incidence of carcinoma of the stomach among the poor is double that in the well-to-do classes, although the total incidence of cancer, which depends upon some unknown constitutional factor, is the same in all classes. This obviously must be the result of some extrinsic cause; it is difficult to believe that it is either the diet or alcohol or tobacco. On the other hand, whereas it is very rare to find anybody among the middle or upper classes without efficient dental plates to replace extracted teeth, it is common to find poor people who have never worn dentures, although for many years they have been edentulous except perhaps for the existence of one or two dirty teeth or stumps. The muscular action of the pyloric end of the stomach has to take the place of mastication in breaking up the food. This results in prolonged friction of the mucous membrane, a very potent factor in the production of chronic gastritis and, in the predisposed, of chronic gastric ulcer—the two precursors of carcinoma, which probably never develops in a healthy stomach (A. F. Hurst, 1939). I have been much struck by the great frequency of edentulous and plateless mouths in the poorest class of hospital patients with carcinoma of the stomach.

Even the best dentures are a poor substitute for natural teeth. Their anchorage is never perfect, they provide only about half the masticatory area, and the height of the tooth cusps and depth of the tooth fissures, upon which the efficiency of mastication depends, are less than half those of natural teeth (F. N. Doubleday, 1943). Moreover the majority of artificial dentures are badly made and inefficient. Consequently the stomach is likely to suffer from the effects of insufficient mastication even when dentures are promptly provided to replace extracted teeth. The frequency with which all or most of the teeth are extracted in young people, especially among the poor, is particularly unfortunate, since the irritation of the gastric mucous membrane by insufficiently masticated food is then prolonged over many years.

The relative incidence of gastric and of duodenal ulcer.—There is a remarkable difference between the relative incidence of gastric and of duodenal ulcer in private and hospital

practice. Whereas they are equally common in hospital, at any rate in London, duodenal ulcer is about four times as common as gastric ulcer in the middle and upper classes in all parts of Great Britain (G. A. M. Lintott, 1936). This is due probably to a higher incidence of gastric ulcer among the poor (resulting from the same extrinsic causes as in carcinoma), duodenal ulcer, which depends mainly upon constitutional and nervous factors, being equally common in all classes. Tidy (1943²) has drawn attention to the steady increase in the incidence of gastric ulcer from 1920 to 1930, after which it remained constant, without any corresponding rise in the incidence of duodenal ulcer. This, I think, may have been the result of the wholesale dental extractions which were made after the introduction into Great Britain from the United States of America in 1920 of the idea of focal sepsis and of dental infection as the main cause of fibrositis, rheumatoid arthritis, gastro-intestinal disorders and many other diseases. Thus unfortunate craze reached its height about 1930 and has begun to recede only during the last two or three years. It would influence the incidence of gastric ulcer only in the poor, many of whom, unlike the well to do, were unable to replace their lost teeth by dentures.

Much has been said about free dental treatment of all children and of adolescents in the future, but little attention has been directed to that of older people. At present the poor, whether they are treated by dentists in private or contract practice or in out-patient departments (except those of hospitals with dental schools), rarely receive any conservative treatment, but are subjected to extractions, a very large proportion of which are quite unnecessary, especially among the young. Those who cannot afford to buy dentures and who do not belong to any insurance scheme by which they are supplied, have their stomachs exposed to constant mechanical irritation year after year, this resulting first in chronic gastritis and chronic gastric ulcer and eventually, in predisposed persons, to carcinoma of the stomach (Hurst, 1939). A great increase in the number of available dentists who are skilled in conservative as well as in radical treatment of dental disease, and financial help in procuring dentures without delay for all who require them, should at least reduce the incidence of chronic ulcer and carcinoma of the stomach in the poor to the much lower level found in the well to do.

ALUMINIUM HYDROXIDE IN THE TREATMENT OF ULCER

Clinical advantages

In recent years magnesium trisilicate and aluminium hydroxide ($\text{Al}_3(\text{OH})_6$) have to a large extent replaced the alkalis formerly used in the treatment of peptic ulcer, since they never give rise to alkalosis, which is an occasional sequel to the administration of the common alkaline powders when given in excessive dosage or for very long periods. Moreover, unlike sodium bicarbonate and magnesium oxide and carbonate, they do not stimulate the secretion of more acid after neutralization of all the free acid present at the moment, because they never lead to complete neutralization. M. J. Schiffrin and S. A. Komarov (1941) have shown that aluminium hydroxide (commonly given in the form of aludrox) has the advantage over magnesium trisilicate in inhibiting peptic digestion in addition to buffering acid, so that the peptic activity of the gastric juice, which is still slightly acid, is inhibited. This is a real advantage in the treatment of ulcer, as the ill effect of gastric juice, although in part due to the high acidity when hyperchlorhydria is present, is in part also a result of the digestive power of pepsin, which is as active with a low degree of acidity as with hyperchlorhydria. Schiffrin (1940) has shown experimentally that aluminium hydroxide is effective in preventing the production of experimental jejunal ulcer in animals.

CARCINOMA OF THE CAECUM AND ASCENDING COLON

Clinical picture

Carcinoma of the caecum and ascending colon presents a very different picture from that of carcinoma of the more distal parts of the colon. Owing to the wide lumen and semi-fluid consistence of the contents, obstructive symptoms occur only in the latest stages of the disease unless the ileo-caecal sphincter is involved. Although discomfort may be present in the right iliac fossa, in the majority of cases there are not any localizing symptoms. Anaemia, which may be extreme, is present in 70 per cent of cases and often gives rise to fatigue and to shortness of breath on exertion before any other symptoms have appeared. It is not the result of massive haemorrhage, which is very rare, and although occult blood is always present in the stools no more blood is lost than in other growths of the alimentary tract in which anaemia may be slight or

completely absent. It is presumably the result of absorption of haemolytic toxins produced in the semi-fluid contents of the caecum. This is not the result of stagnation, which is generally absent, so it must be caused by bacterial decomposition of secretions from the ulcerated surface of the growth, which often attains a considerable size before it is recognized, in contrast with the comparatively small growths which are sufficient to produce obstructive symptoms in the narrow descending, iliac and pelvic colon. A tumour is palpable much less often than in carcinoma of the iliac and pelvic colon or of the rectum, and there is rarely any tenderness.

Diagnosis

The possibility of carcinoma of the caecum or of the ascending colon should always be considered in the presence of unexplained hypochromic anaemia, even in the absence of abdominal symptoms. The diagnosis becomes progressively more probable with increasing age, and the association of the above type of anaemia with right-sided abdominal discomfort is more probably due to carcinoma than to any other disease. Among 170 cases in which resection of the ascending colon and terminal ileum was called for, 112 were of carcinoma, fifty-three were of regional ileitis which generally but not always occurs at a much lesser age, and only four were of tuberculosis (F. H. Lahey and E. Sanderson, 1942). A diagnosis can almost invariably be made with the X-rays, if examinations are made both after an opaque meal and an opaque enema, and if lateral as well as anterior-posterior radiographs are taken to demonstrate growths on the posterior wall. J. H. Ryffel and W. W. Payne (1923) showed how important is the spectroscopic in addition to the chemical examination of the stools for occult blood, because acid haematin is constantly present in carcinoma of the colon, in contrast with the much more common presence of haematoporphyrin in bleeding from the stomach and duodenum. It is of course essential that the patient should be on a haemoglobin-free and chlorophyll-free diet, and that no stool should be examined until the charcoal taken when the diet is changed has all been passed.

Operative treatment

Lahey found that many patients, with conditions thought to be inoperable on account of direct invasion of other structures, can be successfully treated by removal of the latter with the primary growth. The lymphatic glands are often not involved and the patient may survive for many years. Direct spread is most commonly into the ileum, lateral peritonaeum and abdominal wall, but the jejunum, the gall-bladder, the liver and even the kidney may be involved when the growth is in the hepatic flexure. Lahey reports that 57 per cent of his patients with carcinoma of the caecum or ascending colon, who survived excision, lived for five years or more in comparison with 43 per cent in his rectal cases.

INFECTIVE HEPATITIS

The following description of infective hepatitis is written with Col. H. B. F. Dixon, A.M.S., from his personal observations in Malta and England, together with a study of the recent literature and personal communications from officers serving in North Africa and elsewhere.

Aetiology

Infective hepatitis has become increasingly common in the last fifteen years, both in Great Britain and abroad (E. R. Cullinan, 1939). It is now the most important infection in the British Army in North Africa, Malta, Syria and Palestine. The high incidence among British troops in Malta (11.5 per thousand in 1940) is in striking contrast with the low incidence (0.7 per thousand) among Maltese troops (H. B. F. Dixon). Infective hepatitis is also common in the United States of America and in Iceland and widespread epidemics have occurred in the German army on all fronts and in the occupied countries (K. Gutzeit, 1942). The disease should be called infective hepatitis rather than epidemic or catarrhal jaundice, because it is certainly infective in origin, and actual inflammation of the liver is always present. This has been proved by puncture biopsies of the liver by J. McMichael in Great Britain (1943), confirming earlier work in Scandinavia, which demonstrated that the necrosis found at necropsy is mainly a result of post-mortem changes (K. Roholm and P. Iversen, 1939). The old name of catarrhal jaundice should be used only when the jaundice is the result of obstruction of the mouth of the common bile-duct secondary to duodenal catarrh and the liver is not primarily involved. Catarrhal obstruction appears to have been at one time the cause of many of the sporadic cases seen in Great Britain (A. F. Hurst

and C. K. Simpson, 1934), although it has become very rare in recent years, and it was also probably the cause of the epidemic jaundice in Gallipoli in the war of 1914–18 (Hurst, 1943). Infective hepatitis is a better name than infective jaundice, since many cases occur during epidemics which are so mild that no jaundice develops (C. E. Van Rooyen and I. Gordon, 1942). In the present war there has not been any outbreak of spirochaetal jaundice which in the war of 1914–18 was the cause of a large majority of the cases of jaundice in France.

Pathogenesis

The virus agent.—The specific infective agent of infective hepatitis has not been discovered, but it is believed to be a virus which is disseminated by droplet infection, often by healthy carriers and by patients with subclinical attacks. It is often possible to trace contacts. The long incubation period of the disease, the immunity after an attack, the occurrence of subclinical attacks which confer immunity and the absence of leucocytosis all point to a virus infection. In the hepatitis occurring after serum injections the inflammatory material can pass through bacteria-trapping filters and can withstand the action of phenol and freezing, although it is destroyed by heat, and it can be propagated in serum-tyrode-chicken-embryo-medium. Thus it behaves like a virus, although further investigation of its nature is handicapped by the failure to transmit it to any animal. There is no doubt that alcohol lowers the resistance of the liver to infection with the virus of infective hepatitis. This probably explains the much higher incidence in officers than in other ranks, and in men than in women. In Malta in 1940 it was 40 per 1,000 in officers compared with 11·5 in men, and out of 600 cases seen not more than twenty or thirty were in women (Dixon), although the incidence in children in Great Britain is the same in both sexes.

The disease is probably infective only during the few days before the jaundice appears. Consequently there is never any cross-infection in medical wards to which patients with jaundice are admitted, although it is common in surgical wards when patients are admitted in the pre-icteric stage for supposed surgical conditions such as appendicitis or pyelitis, and in wards in which cases are admitted for supposed sand-fly fever before the appearance of jaundice (Dixon). The incubation period is usually from three to five weeks with a minimum of three weeks. In the infective hepatitis occurring after treatment with arsphenamine and with inoculation of vaccine containing human serum the incubation period is longer, generally between six and eighteen weeks.

Symptoms

In very mild cases jaundice is the only symptom, sometimes with malaise and anorexia in addition for a few days. The illness generally begins with headache, pains in the limbs and malaise with fever. The initial symptoms closely resemble those of sand-fly fever, but the headache is less severe and is less often localized in the eyes. Anorexia is always present and is often profound; it is generally accompanied by nausea, but vomiting is uncommon. The patient has a nasty taste in his mouth and has no desire to smoke. There is no herpes labialis. Abdominal discomfort, especially in the epigastrium and in the hepatic region, is very common. The temperature is generally raised for from three to six days. In from one to eight days after the onset jaundice develops and the pre-icteric symptoms and fever rapidly disappear. The stools are always pale and the urine contains bile, which can generally be found one or two days before the appearance of jaundice. Men reporting sick with abdominal symptoms during an epidemic of jaundice should therefore have their urine examined for bile. The jaundice persists for from five to seventy days with an average of three weeks. For two or three days before its appearance, and in cases in which clinical jaundice is absent throughout the illness, the wheal produced by the intradermal injection of 0·25 cubic centimetre of 1 per cent histamine is discoloured yellow (O. Klein, 1931). The rapid pulse of the pyrexial period is replaced by bradycardia, and depression is common as long as the jaundice lasts, but pruritus is rare. The liver is generally tender and is harder than normal; it is enlarged in about 60 per cent of cases. It often remains enlarged after the urine is bile-free and when the jaundice has disappeared. The icteric index remains high for some time after apparent recovery, indicating that the liver is still abnormal. This may be associated with considerable enlargement of the liver, with final recovery in from three to five months. The spleen is enlarged and harder than normal in about 30 per cent of cases. Leucopenia with relative lymphocytosis is common and there is never leucocytosis. Slight anaemia may develop. Haemorrhages

do not occur. Relapses are rare; they are more common in Great Britain than overseas. They are generally more severe than the original attacks and are almost invariably the immediate sequel of indulgence in alcohol. Second attacks are rare. No deaths occurred in Palestine or in Malta and very few in North Africa and in Great Britain. In all fatal cases advanced necrotic changes in the liver were found *post mortem*.

Post-arsphenamine jaundice

Incidence and causal factors.—Concurrently with the world-wide increase in the incidence of infective hepatitis since 1939, there has been a striking rise in the number of patients developing jaundice during arsphenamine treatment for syphilis. In a series of 1,965 soldiers treated for syphilis between 1940 and 1943, 297—or 15 per cent—developed jaundice (D. J. Campbell, 1943,¹ 1943²). In 46 per cent the jaundice occurred during or immediately after the first course of treatment, in 37 per cent it occurred during the second course, and in the remainder during the third or fourth course. The clinical and pathological features of such cases admitted into the same wards at the Connaught Hospital, London, as were patients with infective hepatitis were indistinguishable from the afebrile form of the latter (Dixon), and J. McMichael (1943) found that the pathological appearance of the liver in biopsy specimens was identical. The fact that less than 3 per cent of the patients with jaundice also developed dermatitis, and that none had albuminuria, shows that arsenical poisoning is not the sole cause of the hepatitis. The recent rise in the incidence of jaundice in patients undergoing antisyphilitic treatment is probably due to the increased proneness to infective hepatitis which results from the toxic action of syphilis on the liver, and from treatment with arsenic which is also a liver poison. The vulnerability of the liver is perhaps further increased by some vitamin deficiency due to war-time lack of cheese, milk and butter, and in some cases by the toxic effect of alcohol. The prognosis is good, but it is unwise to give further arsenic injections however completely the patient may appear to have recovered from the hepatitis.

Serum jaundice

A very serious outbreak of jaundice occurred after the use of yellow fever vaccine made with human serum in Brazil in 1939 and in the United States of America in 1942 (J. P. Fox, C. Manso, H. A. Penna and M. Para, 1942). In the Brazilian outbreak there were 1,072 cases with twenty-four deaths, in the American 28,585 cases with sixty-two deaths. The vaccine was essentially the same as that which had been used for several million inoculations since November, 1937. The clinical features of the illness closely resembled those of the afebrile form of infective hepatitis, except that the incubation period was prolonged to from six to eighteen weeks. The temperature was usually normal or was only slightly raised and there was no leucocytosis. Joint pains, urticaria and enlargement and tenderness of the liver each occurred in 20 per cent of the American cases. Only 0.2 per cent ended fatally, generally from two to six weeks after the onset. Recovery was generally complete in from four to eight weeks and permanent liver damage was rare. In fatal cases lesions similar to those found in infective hepatitis and arsphenamine jaundice were discovered, together with marked oedema of the gastro-intestinal tract, enlargement of the spleen and haemorrhages in serous membranes. A similar epidemic occurred in England in 1937 in several scattered groups of children after inoculation with measles convalescent serum coming from a single presumably contaminated source (A. S. MacNalty, 1938). Jaundice developed in thirty-seven out of about 100 patients receiving the serum, and seven died.

Treatment of infective hepatitis

Experimental observations on animals with infective hepatitis and clinical observations on the disease in human beings indicate that a diet containing abundant carbohydrates and proteins with a minimum of fat and with abundant fluids is the most suitable. In the rare cases in which vomiting occurs or when the patient is too drowsy to take sufficient fluid, normal saline alternating with 10 per cent dextrose solution should be given intravenously by the drip method. The patient should not be allowed up until bile is no longer present in the urine, and until the jaundice has completely disappeared and the liver and spleen are no longer palpable. After recovery the patient should be advised to remain teetotal for at least a year, and thereafter he should always be very moderate, invariably avoiding the taking of strong alcohol on an

empty stomach, since the liver is likely to be permanently more vulnerable than normal and is consequently more liable to become cirrhotic even with a comparatively moderate consumption of alcohol.

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BACTERIOLOGY

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Recent advances which bear directly on practical medicine have been concerned chiefly with methods of demonstrating causal agents—some previously unknown—and with elucidation of their sources, routes of entry into the host and modes of spread. The result is that there is an increased effectiveness of measures for prevention by hindering access of the parasites to susceptible individuals. Further evidence has been contributed, by laboratory investigations, that various specific infective organisms have a much wider distribution and persist for a longer time in the body than would be expected from the clinical observations made. On the other hand, grounds have been given for caution in the acceptance for all conditions of purely serological criteria as evidence of present or past infection.

BACILLARY DYSENTERY

Laboratory investigations

New culture media.—Until recently only in the early stages of an attack was the demonstration of the causal organisms in the stools fairly certain, but since the work of F. Telford (1935) was published, agar media containing sodium desoxycholate, sodium citrate and sodium thiosulphate with ferric citrate, lactose and neutral red have been introduced. These media are not difficult to prepare (M. Hynes, 1942), they have the property of suppressing the growth of lactose-fermenting coliform bacilli usually most numerous in the faeces, while permitting the dysentery bacilli to flourish, as well as other specific intestinal pathogens. By this means it has been found that in convalescence recovery of dysentery bacilli from the faeces can be made five or six times more often, and also during a longer period, than by the older method of plating on MacConkey's agar medium.

Incidence.—The persistence of bacillary dysentery in institutions and its repeated recrudescence have always been striking features. Thorough investigation by A. V. Hardy, R. L. Shapiro, H. I. Chant and M. Siegel (1942) of the events in an institution for mentally defective children has shown that of those originally infected with Sonne's bacillus (220 in all), in forty-eight (22 per cent) the disease was clinically recognizable, of seventy-six cases of reinfection discovered however subsequently, only three patients (4 per cent) had symptoms. Thus there was a marked difference between the response made by the individual to the first and the response made to subsequent infections. Reinfection was considered to have occurred when the specific bacilli were again recovered from the faeces after three consecutive negative examinations at two-weekly intervals or four at weekly intervals had been recorded. It seems doubtful, however, whether or not such a series of negative results is conclusive evidence that the bowel no longer harboured the bacilli (See also *Emergency Public Health Laboratory Service Bulletin*, 1942.) J. Watt, A. V. Hardy and T. De Capito (1942), working in similar institutions, found that the ratio of clinical to subclinical (carrier) infections with Sonne's bacillus was 1 : 24, and with Flexner's bacillus 1 : 7. Accordingly, infection with dysentery bacilli may be much more protracted and more widely spread than could be suspected apart from having bacteriological evidence. These circumstances would account satisfactorily for the appearance of a group of further acute cases occurring among patients shortly after their admission to an institution. It is clear that the situation should be dealt with by rigorous bacteriological control in order to detect those who are infected, and also by chemotherapy with drugs such as sulphaguanidine and sulphasuxidine, these being used with the aim of cutting short the carrier state.

THE ENTERIC FEVERS

The typhoid bacillus

New types of organism.—J. Craigie and C. H. Yen (1938¹), (1938²) showed that the typhoid bacillus, long accepted as a single homogeneous species, can be divided into well-defined types by means of bacteriophages acting specifically on the Vi antigens,

which tend to be abundant in recently isolated cultures. When such a phage is propagated continuously on a particular culture of *Bacillus typhosus* it becomes especially adapted and then fails to act on other cultures of the organism. Thus a phage of this kind provides a reagent for detecting whether strains of *B. typhosus* against which it is tested are of the same type as or are different from that to which it has been adapted. So far about twenty different types of *B. typhosus* have been distinguished. A. Felix (1943), during the past three years, has typed over 400 cultures from cases in Great Britain. The epidemiological significance of the findings rests on the fact that patients in any given outbreak of typhoid fever have yielded cultures belonging to the same Vi phage type; furthermore strains from chronic carriers when repeatedly isolated over long periods have not shown any alteration of type, although sometimes they have tended to become 'degraded' and have lost the capacity to be typed by phage. This method of investigation has very considerable epidemiological value when an uncommon type of typhoid bacillus is associated with a series of sporadic cases. Thus W. H. Bradley (1943) has recorded the recovery of a new type (D4) from a man who died in January, 1941 and who at necropsy did not show signs of enteric fever, although blood culture had yielded *B. typhosus*. He had been ill not long before the final illness and was fed on raw milk, contrary to his habits. In the next few weeks eight cases occurred in seven households scattered over an area of about a hundred square miles, and seven of the patients yielded the new type of typhoid bacillus. Excluding four secondary cases, and one which was probably of this nature, a series of eighteen cases occurred over a period of about eighteen months, from thirteen of which the new type of organism was recovered. The milk supply to which the cases were possibly related was derived from four sources, each being itself mixed. The clue finally came from finding that one patient became infected during the time he was working on a farm which contributed milk to one of the sources. The farmer, who did not give any history of illness resembling enteric fever, was observed over a period of three months, during which time *B. typhosus* of the new type was repeatedly recovered from his stools, so that in all probability he was a chronic carrier and the source of infection. This investigation is of interest since it shows that milk-borne typhoid fever infection need not cause an outbreak with 'explosive' characteristics. It also demonstrates that if it had not been for the recovery of an unusual type of the organism from a series of cases, their causal association would probably not have been suspected, and the original carrier might have escaped detection and control for a considerably longer time.

Paratyphoid B fever

Clinical picture and mode of infection—W. Savage (1942) has reviewed his experience of forty outbreaks of this disease and has emphasized the epidemiological differences between it and typhoid fever. In a number of cases the symptoms are at first those of acute food poisoning, but later the same patients develop the enteric picture. Prevalence, at least of outbreaks of multiple cases, in the summer resembles that of salmonella food poisoning. Apart from case-to-case spread, occurring especially in institutions, the vehicle of paratyphoid infection is nearly always an article of food, particularly 'cream'; water and shell-fish are rare vehicles. Of those persons exposed to infection, the proportion attacked is often very low, and therefore explosive outbreaks are uncommon. These peculiarities so far as the vehicle is concerned are attributed to the paratyphoid bacillus not possessing high infectivity, so that invasion of the tissues tends to occur only when there has been a massive inoculum, as when the vehicle is a very suitable culture medium for the organism. Whereas the patient with mild infection or the temporary carrier without symptoms is generally responsible for transmitting the infection, chronic carriers probably play a much less important part than in the transmission of typhoid fever. It is stressed that a comprehensive study of sporadic cases is likely to prove valuable epidemiologically.

POLIOMYELITIS

Epidemiology and aetiology

The virus.—The usual mode of spread of the disease is still not clearly understood. Apart from clinically recognizable cases and from illnesses which bear suggestive characters because they occur in association with an outbreak of poliomyelitis, the specific infection can be detected only by demonstrating the presence of the virus.

At the present stage of technique, this depends on producing paralysis in susceptible monkeys after inoculation with the suspected materials; therefore it is impracticable as a diagnostic measure on a large scale. Accordingly the true distribution of the infection in an affected population must remain largely unknown.

The process of invasion.—Accumulated facts have recently confirmed earlier observations pointing to the importance of the alimentary tract as a route for entry and dissemination of the virus. During the first fortnight of the disease, according to A. B. Sabin and R. Ward (1941), the virus has been demonstrated in the faeces from more than half the number of affected children under eight years of age; this is possible much less often in the case of older individuals. The virus has also been obtained from the faeces of a number of apparently healthy contacts (A. D. Langmuir, 1942). Its presence in sewage has been confirmed at times of epidemics (J. D. Trask and J. R. Paul, 1942). Experimental infection has also been produced in several species of monkeys by feeding them with contaminated material. Thus the important part played by the alimentary tract, as regards both invasion and dispersal of the virus, is evident. It remains to be determined, however, whether the disease is more commonly contracted in this way or from the naso-pharyngeal or respiratory tracts.

Tonsillectomy.—The frequent proportional incidence of the highly fatal bulbar form of the disease after tonsillectomy, has been established by W. L. Aycock (1942). In a collected series of cases occurring within thirty days of the above operation—especially within seven to twenty-one days, which is the incubation period of the disease—the bulbar predominated over the usual spinal form in the proportion of about five cases to one, whereas later—from thirty to sixty days after operation—spinal cases were in excess in nearly the same proportion as they are in the general incidence rates. Thus the conclusion is well founded that there is a causal relation of the local reduction in resistance, 'autarcesis', produced by tonsillectomy to the bulbar form of the disease. The inference is that this operation should not be carried out at seasons of great prevalence of poliomyelitis.

Immunity and immunization

The finding that the serums of a proportion of healthy adults neutralized the virus of poliomyelitis, when tested by injecting a mixture of both serum and virus into monkeys, has been widely accepted as evidence of the prevalence of infection in a community. The serum was believed to acquire the property as a result of the person being infected with the virus and reacting by the production of specific antibody, even although illness did not develop. Doubt has been thrown on the validity of this view by the investigations of F. M. Burnet (1940) made during an epidemic in Victoria, Australia. In certain children who initially possessed considerable antibody to the virus in their serum paralysis nevertheless developed; the antibody in these patients did not increase during the course of the illness. Further, in a number of other patients and contacts observed for several months, no increase occurred in the antibody content of the serum. It appears that immunity to this disease cannot be gauged by the antibody content of the serum. On the other hand, symptomless attacks produced by a modified virus have been shown experimentally to confer immunity (C. W. Jungeblut, Rose R. Feiner and M. Sanders, 1942).

The nature of acquired immunity to poliomyelitis which is present after recovery from an attack is debatable. H. A. Howe and D. Bodian (1941), from their experimental observations on *Rhesus* monkeys, concluded that a second attack seems to depend both on the particular strain of the virus and on the degree to which the virus was disseminated from the neuraxis on the first occasion. They suggested that, in human beings, immunity to poliomyelitis does not result from immunization of the nervous system but is rather the result of some process which prevents infective quantities of active virus from reaching nervous tissue. A. F. Rasmussen, Jun. and P. F. Clark (1942) have pursued this subject further by determining whether or not differences could be shown in the persistence and propagation of poliomyelitis virus along the peripheral nerves of strongly immune as compared with normal monkeys. The immune animals used were either those which had survived an attack from a virulent strain of virus and had resisted a further intracerebral inoculation with the same virus, or those which were first infected with a mild strain of virus and then with a more virulent one. The test inoculation was effected by soaking the proximal end of a freshly cut sciatic nerve in concentrated suspension of virus for several minutes. At

intervals afterwards the inoculated animals were sacrificed, and separate portions of the spinal cord at the cervical and the lumbar levels, as well as of the sciatic nerve proximal to the sciatic notch and at the site of inoculation, were all tested for the presence of virus by intracerebral inoculation into monkeys. Whereas in four out of five normal controls virus was present in the spinal cord after from three to five days, and in the sciatic nerve in three out of eight tests, in none of the five immunized animals was virus demonstrated at any of the sites mentioned above. Thus, while the experiments do not explain the ultimate basis of resistance, they indicate that the latter may be due to the existence of some mechanism for the arrest of the virus intimately associated with nervous tissue.

A suggestive prospect is afforded by the work of C. W. Jungeblut and M. Sanders (1942) who showed that, with poliomyelitis virus, the phenomenon of 'interference' (F. Magrassi, 1935-6; R. Doerr and S. Seidenberg, 1936-7; R. Doerr, and M. Kon, 1936-7) may be obtained; that is, in certain cases two inoculations with virus—the two being made with the same, with related or with different strains—are harmless, whereas one inoculation alone is pathogenic. In this investigation a strain of poliomyelitis virus was used which had been modified by continued passage through mice, and was not any longer virulent for monkeys. This murine virus protected against the development of disease from a virulent strain when the two strains were mixed and were injected intracerebrally into monkeys. The disease was also prevented when the murine strain was injected intravenously either before or after intracerebral inoculation with the virulent virus, each being given in suitable doses and an appropriate interval being allowed to occur between the two injections. The most important of these results from the practical aspect is the therapeutic reaction: the harmless virus, when injected after inoculation with the virulent strain, neutralized the latter. Murine virus heated at 75° C. for half an hour lacks this neutralizing capacity. There is not any evidence that such interference represents an immunity effect; but it may be analogous to the *in vitro* phenomenon observed by C. H. Andrewes (1942)—that growth of an influenza virus in a culture medium rendered the latter unsuitable for supporting subsequent growth of a modified strain, although the medium was without harmful effect on other viruses. The simplest explanation appears to be that the one virus uses up some food-stuff essential for the propagation of the other. The interference phenomenon would then be an instance of the old exhaustion theory of immunity. The possible application in human beings of interference to prophylaxis of poliomyelitis during the incubation period remains for the future.

SWINE INFLUENZA

Aetiology

The reservoir of the virus.—The circumstances in which epidemics originate are still obscure, and of no epidemic is this more true than of that of influenza. Therefore the demonstration of any definite factor must be welcome, even if meanwhile it seems to have little application in the case of the human subject. Pigs in the United States of America suffer from outbreaks of a highly contagious disease which is prevalent in the autumn and is clinically similar to influenza. It is due to a virus closely akin to those of human influenza. When there is an associated infection with *Haemophilus influenzae suis*, a bacillus related to Pfeiffer's bacillus, serious illness results in the pigs, although neither the virus nor the bacillus by itself causes severe effects. But in some instances an attack of influenza was produced in apparently healthy pigs by injection of cultures of the bacillus alone. Proceeding from this point, R. E. Shope (1943), to whose work the discoveries are due, has proved that the virus is present in a 'masked' non-infective form in pigs' lung-worms—a mixed infestation with *Metastrongylus elongatus* and *Choerostongylus pudendotectus*—and is acquired by pigs feeding on earth-worms which harbour the lung-worm larvae. The infection of earth-worms with such virus-bearing larvae occurs under natural conditions. For the activation of the virus in the pig, some provocative stress was required; experimentally this was most readily supplied by giving multiple intramuscular injections of *H. influenzae suis*, but was occasionally furnished in other ways. The masked virus was found in the ova of lung-worms in both the respiratory tract and faeces of pigs. It may also persist in masked form for more than two years in lung-worms' larvae within the body of the earth-worm. When pigs have convalesced after an attack of influenza the infective form of the virus disappears from their respiratory tract, but the masked form may still occur for a time

in the ova of lung-worms which they harbour. Under natural conditions animals may harbour the infection in a latent state; thus in pigs removed to the laboratory from a farm at a time when there had not been any recent outbreak, the disease developed after provocative procedures. Accordingly it is believed that the lung-worm is the reservoir and the intermediate host responsible for the perpetuation of swine influenza virus between one outbreak and the next. The nature of the 'masking' of virus has not yet been determined. The onset of outbreaks of swine influenza in pigs is apparently not related to the time of acquiring the causal virus, but to meteorological or physical influences, since attempts to produce the disease in summer failed regularly.

PRIMARY ATYPICAL PNEUMONIA

The infective agent

Identification of virus strains.—Cases of pneumonia in which the ordinary causal bacteria cannot be recovered from the sputum and other material are believed to be on the increase, at least in the United States of America. The clinical signs are indefinite and blood culture does not yield any growth of organisms. In addition to infections with the rickettsia of Q fever, and with the virus of psittacosis, for several years past there have been a number of instances in which atypical pneumonia developed in people in the north-east states of America, after they had been in contact with cats suffering from a highly infective respiratory tract infection (J. A. Baker, 1942). Mice were inoculated intranasally with suspensions of the lungs of affected cats, and some of them died. Passage of the infective agent through a series of mice was successful, suspensions of the lungs being used as the inoculum, and the virulence of the agent increased. Cultures of a virus were also obtained, eggs being used as a medium. Kittens were infected by intranasal instillation of suspensions of the lungs of affected mice, or of material from inoculated eggs, and developed the typical disease. Elementary bodies similar to those of psittacosis were demonstrated in smears of the mouse lungs and in the egg cultures by means of Giemsa's stain and other methods. Antibodies developed in the serum of infected cats, and the serum gave a positive complement-fixation reaction with suspensions of the elementary bodies; the serum from patients during the acute stage or in convalescence gave suggestive reactions. Practically at the same time M. D. Eaton, G. Meikeljohn, W. VanHerick and J. C. Talbot (1942) reported that some patients with atypical pneumonia yielded an infective agent virulent for cotton-rats (*Sigmodon*, sub-species *hispidus* and *eremicus*) on intranasal inoculation with sputum or lung. It is noteworthy that, in contrast to the findings in Baker's cases, similar material gave negative results on inoculation into mice, ferrets, hamsters and other animals. Moreover, after the virus had become adapted by repeated passages through cotton-rats, the other animals—with the exception of hamsters—still proved resistant to infection. Inclusion bodies, elementary bodies, rickettsiae or visible micro-organisms were not found in sections or in smears of the lungs of affected cotton-rats, when stained with Giemsa's solution or by other methods, and growths were not obtained on ordinary media. The virus passed through Berkefeld N filters, but not readily. By cross immunity tests the identity of six strains was established and the passage virus also produced immunity to inoculation with infective material derived directly from human beings. On the other hand, this virus was distinct from the psittacosis-like virus previously recovered from cases of atypical pneumonia by Eaton, Meikeljohn, VanHerick and Talbot, and also from the other known viruses which are virulent for the cotton-rat on intranasal inoculation.

TRANSMISSION OF INFECTION

Aerial contamination

Disinfection by aerosols and gaseous chemicals.—In infections of the respiratory tract the air is the predominant vehicle. It is obvious that innocuous methods of freeing air from pathogenic organisms will have valuable applications, for example in crowded indoor gatherings or when highly susceptible individuals are collected in groups, as in hospitals. Two methods of disinfection have been used: (1) physical—radiation by ultra-violet light, and (2) chemical—treatment with disinfectants which are suited to act either as mists of fine droplets (aerosols), or in gaseous form. The mode of action of these chemicals may not be the same in all cases since, in contrast to the experience of C. C. Twort and A. H. Baker (1942) that there is an optimum humidity for action

for example with a mixture of hexylresorcinol and propylene glycol, O. H. Robertson, E. Bigg, T. T. Puck and B. F. Miller (1942) stated that propylene glycol used by itself acts as a powerful air disinfectant when in the form of vapour. In a concentration of one gramme of this substance in from two to four million cubic centimetres of air there is immediate and complete sterilization of suspensions of pneumococci, streptococci, staphylococci, Pfeiffer's bacillus, and others, or of influenza virus introduced in the form of a fine spray. The glycol has little toxicity, if any, for higher forms of life, and there remains only the question whether or not ill effects may result after long periods of breathing an atmosphere containing it. The bactericidal action is greatly reduced, for example for haemolytic streptococci, when the humidity is high (W. F. Wells and P. Zappasodi, 1942).

Ultra-violet irradiation.—Although success has been reported in the prevention of childhood infections such as measles, mumps and chicken-pox in schools by ultra-violet irradiation of classroom air (W. F. Wells, M. W. Wells and T. S. Wilder, 1942), it is not to be expected that the results in preventing cross-infections in hospital wards will be readily assessable (H. E. Sommer and J. Stokes, Jun., 1942). As in the case of many other scientific applications in Medicine, it is necessary to accept and to act according to the conclusions drawn from carefully planned experiments (D. G. ff. Edward, Dora Lush and R. B. Bourdillon, 1943). Thus W. Henle, H. E. Sommer and J. Stokes, Jun. (1942) used a large hospital ward divided into cubicles by partitions seven feet high on three sides, reaching from the floor to within four feet of the ceiling, and they exposed mice to an atmosphere into which were introduced virulent haemolytic streptococci or influenza A virus; cultures were atomized in an amount sufficient to cause death of practically all the control animals from the respective infections when the air was not treated in any way. But the mice survived when propylene glycol was vaporized in the proportion of one gramme to from two to five million cubic centimetres of air; they also survived when exposed in cubicles provided with ultra-violet barriers by means of 'germicidal' lamps, installed so as to form three curtains of ultra-violet light, one covering the open front of the cubicle and the other two spread horizontally over the cubicle and the adjoining corridor. The authors point out that this very successful result was obtained when the infective agents were associated with droplet nuclei, that is the floating residue of small droplets after evaporation. Consequently the conclusions need not necessarily apply *in toto* to infective agents associated with larger droplets, or to dust-borne infections, for which other procedures may be required. It is of much interest that lower concentrations of streptococci in the air, which failed to kill the control animals, nevertheless set up in them a latent infection which could be 'activated' by a subsequent superadded inoculation with a virus; on the other hand, in those animals exposed to the treated air, such a condition did not occur.

Bacterial contamination of public eating utensils

Incidence of pathogenic organisms.—M. P. Horwood and P. J. Pesare (1942), in a survey of conditions in public premises which provided solid or liquid refreshment, in Providence, Rhode Island, United States of America, have shown that living haemolytic streptococci and staphylococci could be readily recovered from the ware used to serve customers. *Bacillus aerogenes* was especially common; since it is often present in foodstuffs, particularly cereals, it therefore serves as an indicator of unsatisfactory cleansing of utensils. The possibilities of the transmission of pathogenic bacteria by eating-utensils and drinking-utensils are therefore evident. There is not any reason to suppose that conditions are materially different in similar establishments in other countries or in most institutions. The authors state that 'the most glaring sanitary defect observed during the careful inspection of two large military camps in July, 1941 was the lack of adequate and satisfactory dish-washing facilities'. This work draws attention to the need for concentrating effort upon all possible vehicles of infection.

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ENDOCRINOLOGY

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The most striking advances made in endocrinology during recent years have been in the chemistry of the steroids. The testicular, ovarian and adrenal cortical hormones have been shown to be closely related, in that they possess in common the steroid ring, and the synthesis or isolation of steroid compounds has placed highly active preparations at the disposal of the physician. While much has been achieved by the production of numerous active extracts of the pituitary gland, these demonstrating its many functions, a corresponding advance in this field depends on the isolation of the pituitary hormones. The therapeutics of certain endocrine disorders have been outstandingly successful, but the results of therapy in others have not come up to the expectations which were originally entertained when potent preparations became available.

THE PITUITARY GLAND

Functional activity

Recent work has shown that the belief that the pituitary gland entirely controls the endocrine system is no longer tenable. By virtue of its numerous hormones the pituitary gland exerts a widespread influence but, in spite of this, it forms part of an interdependent mechanism and the considerations referred to below demonstrate that its own activity is controlled by the level of other endocrine secretions. After gonadectomy or in post-menopausal conditions the activity of the anterior lobe is increased, as shown by the greater content of gonadotrophic hormone in the urine and in the gland itself (R. L. Noble, I. W. Rowlands, M. H. Warwick and P. C. Williams, 1939). Whereas small doses of oestrogens stimulate (B. Zondek, 1936), large doses inhibit the activity of the anterior lobe, causing ovarian atrophy with the general effects of hypopituitarism and reducing the amounts of gonadotrophic hormone excreted in the urine and contained in the gland (M. S. Jones and T. N. MacGregor, 1936; I. W. Rowlands and E. P. Sharpey-Schafer, 1940). Zondek has observed that oestrogens inhibit the secretion of the gonadotrophic hormone before they influence the growth hormone, but reports regarding their effect on the thyrotrophic and diabetogenic hormones are conflicting. Histologically, when oestrogens are administered to rats they cause extensive diminution of the secretory chromophil cells of the anterior lobe and occasionally they induce the formation of chromophobe tumours (W. Cramer and E. S. Horning, 1936; Ruth Deanesly, 1939). It may be concluded that the output of gonadotrophic hormone is regulated by the ovaries; when the function of the latter is diminished the result is a removal of the inhibitory influence on the anterior lobe which thereupon elaborates larger amounts of gonadotrophic hormone; this can again be suppressed by the administration of adequate doses of oestrogen. Similarly, in respect of the thyrotrophic hormone, increased functional activity of the pituitary gland results from removal of the inhibitory action of the thyroid gland, and it may be concluded that the thyrotrophic function of the anterior lobe is controlled for the most part by variations in the level of the thyroid hormone.

Antihormones

The formation of substances in the blood antagonistic to the action of an injected hormonal extract has been demonstrated in respect of the thyrotrophic, gonadotrophic, lactogenic and ketogenic hormones. These findings led J. B. Collip (1934) to formulate his hypothesis that the action of certain hormones is antagonized by other so-called hormones; the specific function of the latter is to neutralize the action of the former. There is doubt, however, whether or not such inhibitory substances are in fact hormones, and strong evidence has been brought forward to support the view that antihormones are true antibodies produced in response to injections of heterologous protein.

Various points of clinical interest have arisen from experimental work on the subject. Prolonged courses of injection of gonadotrophic extract into animals of a

species different from that from which the preparation was obtained cause atrophy of the gonads, as a result of the production of a high titre of antagonodotrophic substance in the blood, and injections of antagonodotrophic serum into normal animals cause testicular atrophy in the male and inhibition of ovulation in the female (I. W. Rowlands, 1937). From such observations it must be concluded that the antagonodotrophic substance inhibits the production or the action of the animal's own gonadotrophic hormone. The finding of an increased content of gonadotrophic hormone in the pituitary gland of rats which have been treated by antagonodotrophic serum suggests that the antagonodotrophic substance neutralizes the action of the hormone (R. K. Meyer, H. S. Kupperman and J. C. Finerty, 1942). Similarly a high titre of antagonodotrophic and antithyrotrophic substances is produced in human beings during prolonged treatment by gonadotrophic extract of pregnant mares' serum (equine gonadotrophin) and thyrotrophic extract respectively (I. W. Rowlands and A. W. Spence, 1939; A. W. Spence and L. J. Witts, 1939). Prolonged treatment, therefore, by the pituitary gland and pregnant mares' serum extracts at present available is futile because of the inhibitory substances that are produced and, in respect of pregnant mares' serum extract, the possibility should be borne in mind that gonadal atrophy or damage may be induced. On the other hand, prolonged treatment by gonadotrophic extract obtained from the same species as the animal into which it is injected does not give rise to inhibitory substances. This is also true in the case of a human being injected with extract of human urine of pregnancy (A. W. Spence, E. F. Scowen and I. W. Rowlands, 1938). Since it has been shown that the gonadal atrophy which results from prolonged treatment by certain gonadotrophic extracts is due to the antagonodotrophic substances thus formed, it is most unlikely that gonadal damage would be brought about by the injection of an extract which does not give rise to such substances. Attempts made to utilize antithyrotrophic and antagonodotrophic serums in treatment have been unsuccessful so far.

Hypopituitarism

Simmonds's syndrome.—The pathology of Simmonds's syndrome and of certain forms of hypopituitarism has been clarified by the work of H. L. Sheehan (1937), (1939), (1940) and of H. L. Sheehan and R. Murdoch (1938¹), (1938²), (1939). In women who have had a serious collapse at delivery—usually the result of a severe haemorrhage—and who die during the puerperium, extensive necrosis of the anterior lobe of the pituitary gland may be found, this being due apparently to thrombosis in the vessels. If the patient survives, she may subsequently develop manifestations of severe pituitary insufficiency. Emaciation, hitherto considered to be a cardinal symptom of Simmonds's syndrome, is rare; in fact in most patients the body weight is unaltered. It is probably for this reason that many cases of Simmonds's syndrome are overlooked. On the other hand the majority of patients with emaciation and amenorrhoea who are thought to have Simmonds's syndrome are really the subjects of anorexia nervosa or of some other disease which causes great loss of weight. In women a complicated labour is the commonest cause of Simmonds's syndrome; in men the disease is extremely rare. The smaller pituitary necroses give rise to milder symptoms such as menstrual disturbances, thinning of the hair, debility, anaemia, hypersensitivity to cold, or slight changes in character—symptoms which have long been known to arise after complicated labours. No matter whether the lesion is big or small, a subsequent pregnancy or miscarriage greatly improves or completely cures the symptoms of pituitary gland insufficiency. Sheehan and Murdoch suggest that the improvement is caused by the undamaged part of the gland undergoing normal physiological hypertrophy during the ensuing pregnancy and not returning to its previous size after delivery.

As an aid to the diagnosis of Simmonds's syndrome, R. Fraser and Patricia H. Smith (1941) have utilized the estimation of the urinary excretion of 17-ketosteroids (see p. 54), together with the insulin tolerance test. The 17-ketosteroids are derived from the hormones of the testes and adrenal cortex. Since in hypopituitarism the activity of these organs is greatly reduced, the excretion of 17-ketosteroids is very low in Simmonds's syndrome. Low values may also be obtained in Addison's disease in women and in myxoedema, but the levels are much higher in anorexia nervosa. The insulin tolerance test in Simmonds's syndrome shows the normal initial fall of blood sugar, but an abnormal delay in the subsequent return to the fasting level. This

'hypoglycaemic unresponsiveness' is due to insufficiency of the adrenal cortex, and may therefore occur in Addison's disease but not in myxoedema; it may also be observed in anorexia nervosa. By the combination of the above two tests, Simmonds's syndrome may be differentiated from anorexia nervosa and from myxoedema, two diseases with which it may be confused. Addison's disease, which it may also closely simulate, is distinguished by other features.

Diabetes insipidus

It is now well established, largely through the work of S. W. Ranson and his associates (see below), that the hypothalamus and the posterior lobe of the pituitary gland function as a neuro-hormonal unit in the control of water balance. Destruction of the paraventricular and supra-optic nuclei in the anterior portion of the hypothalamus or of the supra-optico-hypophysial tract, which connects these structures with the posterior pituitary lobe, causes atrophy of the posterior lobe whereas removal of the posterior lobe results in atrophy of the cells of the nuclei. In animals, bilateral lesions in the anterior hypothalamus which destroy the nuclei cause diabetes insipidus (C. Fisher, W. R. Ingram and S. W. Ranson, 1938). It is generally agreed that in man diabetes insipidus originates from a disorder of the hypothalamus or of the hypothalamic-pituitary mechanism. Although removal of the posterior lobe in animals causes diabetes insipidus, total hypophysectomy does not (W. R. Ingram and C. Fisher, 1936), and, in man, a lesion of the posterior lobe causes diabetes insipidus, but this is not produced by a lesion which destroys both lobes. It would appear that the anterior lobe produces a hormone which promotes diuresis, and which may be responsible for the polyuria which is seen occasionally in certain hyperpituitary states. The 'diuretic hormone' may be either the thyrotrophic hormone acting through the thyroid gland (B. O. Barnes, J. F. Regan and W. O. Nelson, 1933) or the adrenotrophic hormone acting through the adrenal cortex (E. L. Corey and S. W. Britton, 1941).

Treatment.—In the treatment of diabetes insipidus the frequency of injections entailed by the use of posterior pituitary extract may be reduced by employing a suspension of pitressin tannate in oil, which is much more slowly absorbed from the site of injection and consequently has a more prolonged action; injections need be given only every twenty-four or forty-eight hours.

THE THYROID GLAND

Hypothyroidism

G. E. Beaumont and J. D. Robertson (1939) have drawn attention to hypothyroidism as a cause of angina of effort. The angina is relieved by the correct dose of thyroid extract but, if the basal metabolic rate is raised above zero, the symptom may reappear. Since angina of effort due to hypothyroidism may arise without any definite evidence of myxoedema, the workers above emphasize that subtotal thyroidectomy for the relief of angina incurs the danger of increasing the symptoms, unless myxoedema and masked hypothyroidism have been excluded. This type of angina is distinct from that which may arise during the treatment of myxoedema with thyroid extract, and which is due to too rapid an increase of metabolism in the presence of sclerosis of the coronary arteries.

Toxic goitre

The pathogenesis of toxic goitre is unknown. In animals the production of hyperthyroidism with exophthalmos by injections of thyrotrophic extract suggested that excessive secretion of thyrotrophic hormone may be responsible for the disease in man. There is not, however, any evidence that there is an increased amount of thyrotrophic hormone in the blood or urine of thyrotoxic patients (S. Hertz and E. G. Oastler, 1936; C. L. Cope, 1938). H. B. Friedgood (1941) still considers that the pituitary gland may be involved for, in discussing the mechanism of exophthalmos, he has suggested that oedema of the orbital tissues is the most likely cause, and that the pituitary gland, which plays an important part in regulating water metabolism, is in some way responsible for the oedema.

THE PARATHYROID GLANDS

Hypoparathyroidism

The tetanic manifestations of chronic hypoparathyroidism are usually well controlled

by calcium and vitamin D. During recent years clinical trials have been made with dihydrotachysterol (A.T. 10), a derivative of tachysterol which is produced by the irradiation of ergosterol and which is closely related to vitamin D. Although it is not antirachitic, its actions are fundamentally similar to those of vitamin D, that is it raises the blood calcium by increasing the absorption of calcium from the gut and the excretion of phosphorus in the urine. Dihydrotachysterol is effective in hypoparathyroidism but has not been found to be superior to vitamin D when the latter is given in equivalent doses (F. C. McLean, 1941).

THE THYMUS GLAND

That the thymus gland produces an internal secretion has been doubted but recent work on myasthenia gravis suggests that this is a possibility. It is well known that the thymus gland is enlarged in the above condition, and that myasthenia gravis very occasionally occurs in conjunction with toxic goitre, in which condition the thymus gland also may be enlarged. Adler (quoted by L. M. Eaton, 1942) claimed that by transplanting the thymus glands of puppies and calves into mature dogs he produced a condition resembling myasthenia gravis which was temporarily benefited by the administration of prostigmin (neostigmine). Removal of the thymus gland is reported to improve some patients with myasthenia gravis (A. Blalock, A. McG. Harvey, F. R. Ford and J. L. Lilienthal, Jun., 1941) and, although too few patients have as yet been treated in this way, the results point to the possibility that the thymus gland may produce an internal secretion which has a curare-like action.

THE SEX HORMONES

The male and female gonadal hormones and the cortical hormones which have been isolated from the adrenal glands are closely related structurally in that they all contain the steroid or cyclopentenophenanthrene ring. This close relationship is reflected to some extent in their reciprocity of action. Testosterone is slightly progestogenic and slightly oestrogenic; progesterone in large doses can maintain the life of an adrenalectomized rat and is slightly androgenic; the adrenal hormone, desoxycorticosterone, is slightly androgenic and slightly progestogenic. It is interesting that testosterone, oestradiol, oestrone and progesterone all cause sodium retention in the normal animal, an action which desoxycorticosterone also has in the adrenalectomized animal. In some species relatively small doses of oestrogen given in conjunction with androgen may enhance the androgenic effect; on the other hand, oestrogens and androgens are mutually antagonistic in action in that relatively large doses of the one inhibit the action of the other (C. W. Emmens and T. E. T. Bradshaw, 1939).

Androgens

A large number of androgens have been prepared, but only six have been found so far to occur naturally. The male hormone, secreted by the interstitial tissue of the testes, is testosterone—the most potent androgen known and the only one which has as yet been isolated from the testes; it is prepared synthetically from cholesterol. There is no evidence that testosterone is excreted in the urine; it appears to be broken down in the body to the much less active androgen, androsterone, and the inactive stereo-isomeric compound aetiocholan-3(α)-ol-17-one, both of which have been isolated from normal male urine (N. H. Callow, 1939). That these substances are products of testosterone is suggested by the observation that their excretion is greatly increased by the administration of large doses of testosterone propionate (N. H. Callow, 1939; R. I. Dorfman and J. B. Hamilton, 1939). Another androgen which has been isolated from normal male urine is *trans*dehydroandrosterone, which has about one-third of the activity of androsterone. The excretion of *trans*dehydroandrosterone is not recognizably increased by the administration of testosterone propionate, which indicates that it is probably not derived from this hormone. The amounts of androgenic substances which have been isolated from urine do not account for the whole of its biological activity.

From the urine of normal women N. H. Callow and R. K. Callow (1939) have isolated the three substances mentioned above—androsterone, aetiocholan-3(α)-ol-17-one and *trans*dehydroandrosterone—in yields approximately equal to those of the same compounds from normal men's urine, showing that their excretion is not an index of the secretory activity of the testes. The substances have also been isolated from the urine of ovariectomized women in yields which are only slightly below those

obtained from normal women's urine (H. Hirschmann, 1939) and from the urine of a eunuch (N. H. Callow and R. K. Callow, 1940). All these observations, together with the failure of testosterone propionate to have any recognizable effect on the excretion of *transdehydroandrosterone*, and the finding by A. C. Crooke and R. K. Callow (1939) of greatly increased quantities of *transdehydroandrosterone* in the urine of patients with an adrenal gland tumour suggest (1) that the substance is derived, not from the gonads, but from the adrenal cortex, and (2) that androsterone and aetiocholan-3(α)-ol-17-one do not originate solely in the gonads in either sex. Although the last two substances are known to be derived from testosterone when this has been injected, it does not follow that their presence in women's urine indicates that testosterone is secreted by women. In both sexes they may be also transformation products of other steroids from the adrenal cortex (Callow and Callow, 1940).

17-ketosteroid assay.—The biological assay of urinary androgens may be carried out by measuring their capon comb growth-promoting activity (C. W. Emmens, 1939¹). It has been stated above that probably merely the degradation products of the original hormones are excreted in the urine and that, in the case of substances derived from testosterone, they possess less activity than the parent substance; in fact, at least one such product is known to be inactive; on the other hand some of the parent substances in the adrenal cortex may not themselves be androgenic. For these reasons biological assay of androgens in the urine is not by any means a specific index of the production or utilization of androgens in the body (N. H. Callow, R. K. Callow, C. W. Emmens and S. W. Stroud, 1939).

An index of the androgenic activity of urine is obtained by the biochemical colorimetric method of N. H. Callow, R. K. Callow and C. W. Emmens (1938). The method is based on the fact that the steroid compounds with a ketone group on the 17th carbon atom (17-ketosteroids), that is substances such as androsterone, aetiocholan-3(α)-ol-17-one and *transdehydroandrosterone*, produce a red colour in the presence of alkali and *meta*-dinitrobenzene. The test does not determine the value of androgenic potency, since it cannot distinguish between active and inactive ketosteroids, but the figures run parallel with those obtained by biological assay. As with the comb growth-promoting method, biochemical assay does not necessarily give any information concerning the degree of androgenic activity in the body. There is a wide variation in 17-ketosteroid excretion, which limits its diagnostic value. According to N. H. Callow, R. K. Callow and C. W. Emmens (1940), normal adult men excrete from 3.5 to 15.0 milligrams (mean 9.05 milligrams) per day, and normal adult women excrete from 1.7 to 12.6 milligrams (mean 6.75 milligrams) per day. In terms of androgenic activity the values range from 6.5 to 110 international units per day for men and from 2 to 50 international units for women. In children before puberty and in old people the excretion is low. In eunuchs the figures obtained by the above workers varied from 3.1 to 10.9 milligrams (mean 7.4 milligrams), in eunuchoids from 3.8 to 16.0 milligrams (mean 8.7 milligrams) and in ovariectomized women from 2.8 to 21.4 milligrams (mean 6.5 milligrams—excluding the anomalous high figure) per day. In treated patients with Addison's disease the values were from 3.5 to 7.5 milligrams (mean 4.9 milligrams) for men and from 2.3 to 9.8 milligrams (mean 5.4 milligrams) for women. It is clear from the foregoing figures that the present methods of assay have little diagnostic value. It is only in certain cases of adrenal cortical tumour, in which very high values are found, that the assays have any real diagnostic significance (see page 54). Since the evidence is strongly in favour of the adrenal cortex being a source of androgens, very low values should be expected in cases of Addison's disease in women, and in pituitary insufficiency in which both the adrenal glands and the gonads are affected.

Oestrogens

The natural follicular hormone, *α -oestradiol*, which was originally isolated from sows' ovaries, has also been isolated from the urine of pregnant mares and pregnant women, and from human placentas. Oestrone is present in the human placenta and in the urine of women and of mares. Oestriol is the principal oestrogen in women's urine, and occurs in the placenta in an amount that is double the combined weights of the oestrone and of *α -oestradiol* (E. A. Doisy, 1942). As *α -oestradiol* is the only oestrogen which has been isolated from the ovaries, it would seem that it is largely converted in the body into oestriol and oestrone. It is well known that oestrogens are present in males; men excrete in their urine the equivalent of about 0.01 milligram of

oestrone daily. Oestrone has been isolated from men's urine and in large amounts from the urine of stallions, and both oestrone and α -oestradiol have been found in the testes of stallions. The origin and function of oestrogens in the male are unknown; since they are decreased in eunuchs, they may be partly derived from testosterone. Such a view is supported by E. Steinach and H. Kun (1937) and by others who observed that the administration of testosterone propionate to men causes increased excretion of oestrogens. There is not any definite evidence that the oestrogenic material is a direct degradation product of testosterone or that it is secreted by some endocrine organ, possibly the adrenal cortex, as a result of stimulation by testosterone (N. H. Callow, R. K. Callow and C. W. Emmens, 1939).

Notable contributions to therapeutics have been the syntheses of two oestrogens which are highly active when given by mouth, namely 4-4'-dihydroxy- α - β -diethylstilbene, or diethylstilboestrol (E. C. Dodds, L. Goldberg, W. Lawson and R. Robinson, 1938) and 4-4'-didydroxy- γ : δ -diphenyl-*n*-hexane, or hexoestrol (N. R. Campbell, E. C. Dodds and W. Lawson, 1938). When given by mouth hexoestrol has approximately the same degree of activity as diethylstilboestrol. As with oestradiol, the effectiveness of diethylstilboestrol is increased by esterification, the most potent ester being stilboestrol dipropionate. Esterification of natural and synthetic oestrogens does not increase their effectiveness when the compounds are given by mouth (C. W. Emmens, 1939²).

Assay.—Determinations of the oestrogenic activity of urine may be carried out by the Allen-Doisy vaginal smear method. The error of quantitative estimation, however, is large and it is further increased by the presence of augmenting, but non-oestrogenic, substances (Emmens, 1939¹). The excretion of oestrogens is much greater in women than in men, and in both sexes it is reduced after gonadectomy, although individual figures come within the range of variation found in normal subjects (Callow, Callow and Emmens, 1940). In normal women the excretion is highest in the middle of the menstrual cycle, at the time of ovulation and before the menses during the period of activity of the corpus luteum, but it drops rapidly just before the menstrual flow begins. It is greatly increased during pregnancy, in women with a granulosa-cell tumour of the ovary, and in most cases of the adreno-genital syndrome. In children the output is low and there is little difference in the levels in the two sexes.

Progestogens

The most important of the progestogenic compounds are progesterone—the natural progestational hormone of the corpus luteum, which is inactive by mouth and an orally active derivative of progesterone, ethisterone (synonyms: anhydro-hydroxy-progesterone, pregnenolone, 17-ethinyltestosterone). Progesterone occurs only in extremely small amounts in the placenta and in the urine since it is completely broken down and inactivated in the body. A degradation product of progesterone has been isolated from the urine as sodium pregnanediol glucuronide by E. H. Venning and J. S. L. Browne (1936), (1937), and E. H. Venning (1937), (1938) has devised a quantitative method for its estimation. The compound is present in the urine only when progesterone is being formed in the body; in the non-pregnant woman it is found only during the luteal phase of the menstrual cycle and it disappears before menstruation begins. The daily excretion varies from 2 to 10 milligrams. It is absent in patients with amenorrhoea and during the cycles of anovulatory bleeding. In early pregnancy the excretion is approximately the same as it is during the luteal phase of the normal cycle, but usually between the seventieth and the eightieth days it begins to rise, and by the seventh or eighth month has reached values of from 60 to 100 milligrams a day. After labour pregnanediol entirely disappears from the urine within twenty-four hours. The estimation of sodium pregnanediol glucuronide is of value in investigating disorders of menstruation and pregnancy, but C. L. Cope (1940¹) challenges the assumption that its excretion reflects quantitative variations in the activity of the corpus luteum.

Sex hormone therapy in the male

Eunuchism.—Testosterone is specific only for the treatment of eunuchism and eunuchoidism, in which it replaces deficiency of an essential hormone. The initial treatment of patients with eunuchism consists of intramuscular injections of testosterone propionate in total doses of from 100 to 200 milligrams per week, or of the intramuscular implantation of a 50-milligram pellet of testosterone or of methyl

testosterone. A pellet of testosterone is completely absorbed in from eight to ten weeks. Potency is rapidly established, but if priapism is frequent the dose may have to be reduced. Although implantation of a pellet obviates the necessity of frequent injections, it has the disadvantage that the rate of absorption cannot be controlled. When the optimum effect has been obtained, recourse should be had to oral treatment by methyl testosterone. The tablets may be swallowed, or better, they may be sucked under the tongue since it is found that, when methyl testosterone is absorbed into the sublingual vessels, a somewhat smaller dose is required—probably because a fraction of the swallowed material is degraded in the liver before it brings about its effect. The maintenance dose by the sublingual route varies from 10 to 30 milligrams daily.

Eunuchoidism.—Pre-adolescent, adolescent and adult eunuchoidism may be caused by primary testicular failure or by hypopituitarism. Differentiation between these two causes is difficult, but stunting of growth suggests pituitary deficiency, whereas increased growth of the long bones suggests primary testicular deficiency. Endocrine therapy for hypogonadism in children should, in general, be avoided. The normal onset of puberty varies widely, and often a boy who appears to have some degree of genital hypoplasia ultimately proceeds spontaneously to normal development. The majority of patients with Fröhlich's syndrome respond to treatment by diet alone and subsequently develop normally. Endocrine therapy is reserved for the severe cases of pre-adolescent eunuchoidism in which specific treatment appears to be indicated. It is preferable to begin with a three months' course of chorionic gonadotrophin in an attempt to stimulate the production of androgen by the interstitial tissue of the testes. Lack of response suggests primary testicular failure and indicates treatment by androgen administration. On the other hand, if a satisfactory response is obtained with gonadotrophin, further courses may be necessary, until perchance the testes are able to function spontaneously. Treatment by chorionic gonadotrophin or by testosterone propionate frequently increases the growth rate of sexually underdeveloped boys. It is unlikely that in cases of adult eunuchoidism the testes can be stimulated by gonadotrophins; for this condition treatment by androgens, as for eunuchism, is usually necessary.

The complications which may arise as a result of androgenic therapy are priapism, excessive genital growth, acne, oedema and gynecomastia. Testosterone propionate causes reduction in urinary nitrogen, sodium, potassium and chloride, and the gain in weight which often occurs is probably due largely to the water held in association with the retained salts and protein (A. T. Kenyon, Kathryn Knowlton, Irene Sandiford, F. C. Koch and Gertrude Lotwin, 1940). The oedema which is occasionally seen is associated with the salt retention.

Psychogenic impotence.—Impotence is due far more commonly to a psychogenic factor than to hypogonadism. A diagnosis of androgenic deficiency should not be made without some evidence of underdevelopment of the secondary sexual characteristics. Androgens are not aphrodisiacs and, when injected, do not stimulate sexual function in the absence of androgenic deficiency, that is in normal subjects or in patients whose impotence is functional.

Prostatic hypertrophy.—Testosterone propionate has now been widely used for prostatic enlargement in man and, although there have been many claims of clinical improvement, there have been as many reports denying such an effect (N. J. Heckel, 1940). It may be stated that there is no scientifically acceptable evidence that testosterone propionate is of permanent value in the treatment of patients with prostatic hypertrophy.

Sterility.—Sterility in the male is a complex subject and entails extensive investigation. Its causes fall into two main groups—urological and constitutional. Constitutional causes, which are the commoner, include endocrine disorders of which the chief are hypothyroidism, hypopituitarism and hypoplasia of the testes. There is, however, a large group of cases in which there is not any apparent cause; in these cases an inherent defect of the spermatogenic tubules may be postulated. Examination of the sperm may show an oligospermia, an increased number of abnormal forms or a normal count associated with a low basal metabolic rate. Fertility depends on the quality rather than the quantity of sperm; oligospermia is not necessarily associated with sterility. As a diagnostic and prognostic procedure C. W. Charny (1940) advocates testicular biopsy. Cases which are due to hypothyroidism respond well to thyroid

extract therapy, but the treatment of sterility due to other endocrine disturbances is purely in the experimental stage. Satisfactory results with gonadotrophic extracts and with small doses of testosterone propionate have been reported by some workers, whereas others have obtained little or no response with such preparations. It is not known why patients who are apparently in the same clinical category react differently to sex hormone therapy.

Sex hormone therapy in the female

For the treatment of gynaecological disorders there are at our disposal the gonadotrophins and the natural and synthetic oestrogens, progestogens and androgens. The synthesis of oestrogens which are potent when given by mouth has replaced the use of the natural product to a large extent, but in some cases synthetic oestrogens have the disadvantage of causing gastro-intestinal disturbances. That androgens should be used in gynaecological states is controversial; lack of space forbids discussion but it should be emphasized that the indiscriminate use of either androgens or oestrogens is to be deplored.

Amenorrhoea.—The management of amenorrhoea remains basically unchanged. In patients with moderate degrees of ovarian failure or of diminished endometrial response, treatment by an oestrogen or by an oestrogen and a progestogen allows the ovaries or endometrium to recover and re-establishes the cycle. In more severe grades of ovarian deficiency, however, their administration, which is merely a replacement therapy, has to be continued year after year and produces only an artificial menstruation. Since the patients remain sterile, there is little to recommend treatment in such cases. The value of gonadotrophins in amenorrhoea is questionable since they do not stimulate the human ovary to any appreciable extent.

Functional bleeding —The cause of functional bleeding is unknown. The explanation that it is caused by the unopposed action of oestrogen, either as a result of its overproduction or of diminished activity of the corpus luteum, is untenable since functional bleeding may be associated with any type of endometrium. R. Kurzrok (1941) has postulated that the primary defect is an inherent disturbance of oestrogen metabolism within the endometrium. In the absence of a known cause therapy is empirical. Thyroid extract is sometimes beneficial. Equine gonadotrophin is of little value; chorionic gonadotrophin, originally employed in the mistaken belief that it promoted the formation of a corpus luteum, occasionally appears to be of benefit, but the general consensus of opinion is that it is unreliable (T. N. A. Jeffcoate, 1937). Good results have been claimed with progesterone and ethisterone, but on the whole these preparations, when used alone, give unsatisfactory results. The combined use of oestrogen and progesterone is reported to be an effective method of regulating bleeding and, in certain patients, of enabling the ovaries to recover their normal function (E. C. Hamblen, W. K. Cuyler, C. J. Pattee and G. J. Axelson, 1941¹). Daily injections of 1 milligram of oestradiol benzoate or dipropionate are started immediately after bleeding has stopped, or failing this, on the seventh day of bleeding, and are continued for from ten to fourteen days; the treatment is followed by a course of 5 milligrams of progesterone and 1 milligram of oestradiol benzoate or dipropionate given every other day for from ten to fourteen days. Subsequent cycles of therapy may consist only of the latter part of the therapy given during the first cycle, that is oestrogen and progesterone during the last ten to fourteen days. At least four cycles of therapy should be given. In one series the results were not quite so satisfactory when ethisterone was substituted for progesterone (Hamblen, Cuyler, Pattee and Axelson, 1941²). It is suggested that oestrogens are necessary for the metabolism and effective action of endogenous and injected progesterone, and that both hormones may correct an endometrial disturbance in steroid metabolism, which in some cases may be the primary cause of ovarian failure.

Testosterone propionate, which probably acts by inhibiting the gonadotrophic activity of the pituitary gland, suppresses ovarian function and consequently also suppresses the menses. Its use in women is considered by some workers to be contra-indicated because of the danger of masculinization, but Kurzrok, and S. H. Geist and U. J. Salmon (1941) find that bleeding can be suppressed by a total monthly dose of from 250 to 300 milligrams which, they state, is insufficient to produce masculinization. Twenty-five milligrams are injected daily or three times a week, and the total dose is either distributed throughout the entire cycle or is given during the first ten

days of the cycle. If any regressive changes characteristic of oestrogen deficiency appear in the vaginal smears, which are taken twice a week, therapy is stopped. If there is not any improvement in the menstrual period, the course is repeated during the next month.

Dysmenorrhoea.—The cause of this condition is also unknown. It has been ascribed to an excess and to a deficiency of oestrogen, to an excess and to a deficiency of progesterone and to a neurosis. Treatment by oestrogen is favoured by some observers, and may be of benefit if there is an associated uterine hypoplasia. Other workers consider that the most effective remedy is testosterone propionate, which is given by some clinicians in doses of 25 milligrams twice a week throughout the cycle, and by others in doses of from 5 to 10 milligrams on alternate days, starting on the day before the usual onset of pain. The results of treatment with progesterone are inconclusive. It is highly probable that the psychogenic factor is the most important.

Threatened and habitual abortion.—Threatened abortion is often associated with a greatly diminished excretion of sodium pregnanediol glucuronide, indicating failure in the production of progesterone and providing the rationale for its use in treatment. It should be given in doses of from 5 to 10 milligrams daily. For women who have aborted frequently in the past, 10 milligrams of progesterone are given twice a week from the second to the fifth month of pregnancy, and the treatment should be supplemented with ethisterone given daily by mouth in doses of 15 milligrams. The value of this treatment is difficult to assess since such women may go to term without any therapy. On the other hand progesterone is ineffective in many cases of threatened and habitual abortion, probably because the embryo is abnormal (J. S. Henry, E. H. Venning and J. S. L. Browne, 1938). The pregnanediol output is not an infallible indication whether abortion will or will not take place (C. L. Cope, 1940*; A. M. Hain, 1942). Abortion may occur in the presence of a normal output of pregnanediol and pregnancy may proceed normally in the temporary absence of any pregnanediol excretion in the early stages.

Sterility.—The treatment of sterility due to the absence of ovulation is still in the experimental stage. M. E. Davis and A. K. Koff (1938) claimed to have brought about ovulation in normal women by giving intravenous injections of equine gonadotrophin but the results in sterile women have been disappointing, probably because there is some degree of hypopituitarism and a consequent deficiency of an augmenting factor. Augmentation or synergism of equine gonadotrophin may be obtained with chorionic gonadotrophin, and encouraging results have been reported with the use of the two extracts in sequence (E. C. Hamblen, W. K. Cuyler, J. A. Wilson and R. L. Pullen, 1941).

Mammary glands.—(1) Mastopathia. When pain in the breast is due to mastopathia and is not of psychogenic origin, it is postulated that it is caused by distension of the ducts and acini brought about by the action of oestrogens. Before initiating hormone therapy a psychogenic factor should be excluded by administering a placebo. Testosterone propionate often relieves the pain, and sometimes reduces the size of the nodules if these be present but, because of the danger of masculinization, parenteral therapy should not be recommended. This complication is avoided by the local inunction of from 4 to 10 milligrams of testosterone daily, which usually affords relief. When the pain is pre-menstrual treatment should be started a few days before the usual date of onset. Progesterone is also reported to be of benefit, but oestrogens aggravate the condition. (2) Lactation. (a) Induction of lactation. The problem of the hormonal control of lactation is complex; it is generally considered that a specific hormone of the anterior pituitary lobe is mainly responsible since injections of an anterior pituitary extract (prolactin) initiates lactation in the intact female animal. Prolactin has been used in women to stimulate the secretion of milk after parturition, with conflicting results. S. J. Folley and F. G. Young (1940) do not think that prolactin is a specific lactogenic hormone. Anterior pituitary extracts which are able to initiate lactation also possess the property of causing enlargement of the pigeon's crop gland, and it is widely believed that the two effects are due to the action of one hormone, prolactin. Preparations of prolactin are therefore assayed in terms of their crop-stimulating activity. Folley and Young have shown that injections of crude anterior pituitary extracts cause a greater yield of milk in cows with declining lactation than do purer preparations which contain seven times as much prolactin (crop-stimulating) activity. They consider that this 'galactopoietic' power depends on the cooperative action of prolactin and

some other anterior lobe hormone, and that the crop gland test (that is prolactin content) is not a measure of galactopoietic activity. In view of their results they feel that the lack of agreement about the clinical efficiency of prolactin is not surprising (Folley and Young, 1941). The local application of diethylstilboestrol induces copious lactation in virgin goats and heifers, possibly acting by stimulating the pituitary gland (S. J. Folley, Helen M. S. Watson and A. C. Bottomley, 1940, 1941).

(b) Inhibition of lactation. Oestrogens and androgens have been used extensively to inhibit lactation and to relieve the pain and tenderness of engorged breasts. J. Meites and C. W. Turner (1942), however, have wisely pointed out that, in almost all reports on the successful inhibition of lactation with oestrogens and androgens, the babies were removed from the breast simultaneously with the administration of the hormones and that, since the maintenance of lactation depends on the nervous stimulus of suckling, milk secretion under such conditions would soon cease even in the absence of hormone therapy. In support of their criticism they quote the work of A. R. Abarbanel and M. J. Goodfriend (1940) and of Abarbanel (1941) who allowed the mothers to suckle their babies during the period in which they were receiving large doses of androgens or oestrogens, which failed to inhibit lactation. The relief of the painful breast enlargement which is brought about by hormone therapy is not synonymous with inhibition of lactation, since breast engorgement is due, not to filling of the breast with milk, but to venous and lymphatic stasis.

Sex hormone therapy in either sex

Oestrogens are reported to be of benefit in buccal leucoplakia (I. T. Nathanson and D. B. Weisberger, 1939) and in atrophic rhinitis (W. W. Eagle, R. D. Baker and E. C. Hamblen, 1939; I. S. Hall and I. A. M. MacLeod, 1942), and oestrogens or testosterone propionate have been used in otosclerosis (J. Bernstein and L. Gillis, 1939). Reports of therapeutic trials of sex hormones in the above conditions are scanty, and further work is necessary before any definite assertions can be made.

THE ADRENAL GLANDS

Adrenal gland hormones

More than twenty-five crystalline compounds which contain the *cyclopentenophenanthrene* system have been isolated from the adrenal cortex but, in spite of this, they by no means account for the whole of its activity and it is doubtful whether or not any of them is the true adrenal cortical hormone. Those which are capable of giving rise to one or more of the actions of the adrenal cortex are corticosterone, 11-dehydrocorticosterone, 11-dehydro-17-hydroxycorticosterone, 17-hydroxycorticosterone, 11-deoxycorticosterone and 11-deoxy-17-hydroxycorticosterone. Other compounds include oestrone, progesterone, 17-hydroxyprogesterone and adrenosterone, which is slightly androgenic. The remaining substances have not been shown to have any biological activity. There is also evidence that the cortex contains an additional principle which causes retention of sodium, and another derivative which is concerned with lactation.

Desoxycorticosterone (21-hydroxyprogesterone), which has been synthesized, is the most active of the compounds isolated, in its ability to maintain life. E. C. Kendall (1941), however, has described the preparation from adrenal extracts of an 'amorphous fraction' which has greater activity, but his work has not been confirmed. Desoxycorticosterone also regulates the electrolytic balance by decreasing the excretion of sodium and increasing the output of potassium, but it has little influence on carbohydrate metabolism. The potency of desoxycorticosterone is increased by esterification, the most effective ester being the acetate.

Corticosterone, which has also been synthesized (T. Reichstein, 1942), is the next most active compound. It does not maintain the life of an adrenalectomized animal as effectively as does desoxycorticosterone, and its power of causing sodium retention is less, but it increases the work capacity of adrenalectomized animals to a greater extent than does desoxycorticosterone and has a much greater influence on carbohydrate metabolism. Its effects, however, on the hypoglycaemia of Addison's disease are not sufficient to be of any practical value. Dehydrocorticosterone has actions similar to those of corticosterone.

Treatment of Addison's disease

Salt and, for patients who require it in addition, desoxycorticosterone acetate is

effective in and is the cheapest form of treatment of this disease. Some observers, however, have found desoxycorticosterone acetate less reliable than cortical extract. Although a low level of potassium in the diet is beneficial and reduces the requirement of hormone, it is generally agreed that it is rarely necessary. In patients who are not in a crisis, sodium chloride in doses of from 6 to 12 grammes (90 to 180 grains) daily should first be tried, since hormone may not be needed. If the results are not satisfactory, from 2 to 5 milligrams of desoxycorticosterone acetate in oil (or from 5 to 10 cubic centimetres of cortical extract) a day are given and, if there is not any gain in weight during the next few days, the dose is gradually increased. G. W. Thorn (1941) and other workers are of opinion that with desoxycorticosterone acetate not more than 5 grammes (75 grains) of salt a day should be given in order to prevent oedema. S. L. Simpson (1939) and H. W. Dryerre (1939) were among the first to report that the implantation of tablets of desoxycorticosterone acetate brings about a prolonged improvement. Thorn has described the details of this form of therapy. It is important that implantation should not be done until the daily requirement of desoxycorticosterone acetate has been determined accurately and the patient is taking a constant amount (5 grammes per day) of salt. For each 0.5 milligram ($\frac{1}{40}$ grain) of desoxycorticosterone acetate that is required during twenty-four hours, one pellet of 125 milligrams (2 grains) is implanted, and the salt intake remains unchanged. The use of salt provides a convenient means of balancing any possible excess of hormone. If the amount implanted proves to be too great, salt is withdrawn and, if necessary, a salt-free diet and potassium citrate are given. Pellets of 125 milligrams meet the requirements for from nine to twelve months. When symptoms recur after absorption, the salt should be increased and, if this is inadequate, desoxycorticosterone acetate is given by injection, the patient is 're-balanced' and a further implantation is made. During periods of stress, such as in an associated secondary infection, supplementary injections of desoxycorticosterone acetate may be necessary. In the treatment of a patient in an adrenal crisis desoxycorticosterone acetate should be supplemented by cortical extract. The sublingual administration of a propylene glycol solution of desoxycorticosterone acetate has recently been tried for chronic Addison's disease, but has been less effective than injections or implantation (A. Wilson, 1942).

The adrenogenital syndrome

S. L. Simpson, P. de Fremery and A. Macbeth (1936) demonstrated that excess of androgens is excreted in the urine of patients with the adrenogenital syndrome. Since then all investigators are agreed that the excretion of androgens is increased in this condition, and that the estimation of urinary 17-ketosteroids is an important procedure in the diagnosis of an adrenal cortical tumour. The output of ketosteroids in post-pubertal cases of tumour varies from 40 to 325 milligrams or more per day. Their excretion falls to normal after operation for removal of the tumour. Crooke and Callow showed that the excess of androgenic activity is mainly accounted for by large amounts of *trans*dehydroandrosterone. Since this substance has but slight androgenic activity, it is possible that it is a degradation product of some more potent androgen which is produced by the adrenal glands. Jocelyn Patterson, Isobel M. McPhee and A. W. Greenwood (1942) have studied 17-ketosteroid excretion in various types of adrenal virilism. They found that, in children before puberty, it is impossible to differentiate solely on the basis of the ketosteroid output between adrenal hyperplasia and adrenal tumour, since in both conditions high excretion values are obtained. Although young children with virilism or with sexual precocity (with or without a tumour) may excrete well below 40 milligrams per day, the output is far in excess of that of normal children in the same age group. In older children with pre-pubertal virilism associated with adrenal hyperplasia, the output may be well above 40 milligrams per day and, in view of this, the above workers feel that 100 milligrams is the lowest figure which can be safely considered to be diagnostic by itself of an adrenal tumour in this type of case. In post-pubertal virilism or in hirsutism unassociated with a tumour, the excretion may be normal or increased, but it does not rise above 35 milligrams per day. A. Grollman (1939) has suggested, as an explanation of adrenal virilism, that the disorder is due to the inclusion of embryonic androgenic tissue during development or to a perversion of the normal metabolism of the gland, so that the diseased organ produces an androgen instead of the chemically related cortical hormone.

CONCLUSION

From the foregoing it will have been seen that, apart from the discovery of acute necrosis of the anterior lobe of the pituitary gland as a cause of Simmonds's syndrome, no fundamental knowledge has been gained recently of the basic aetiology of glandular dysfunction. It should be realized that treatment is limited to making good a deficiency or to removing the source of excessive secretion. In the majority of cases it is not possible to treat the fundamental cause of the disorder. Above all it is necessary that the remedies used should be given in adequate doses for the appropriate disease, and that they should not be given indiscriminately for conditions which have no recognizable connexion with a hormonal disturbance.

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ACUTE INFECTIVE DISEASES

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NATIONAL HEALTH

Despite the adverse effects of the direct stresses of war and the indirect strain caused by a steady depletion of medical and nursing staffs, the national health remains satisfactory. The health services have been proved to be sufficiently flexible to cope with the various difficulties of reorganization and adjustment made necessary by the evacuation from and return to their homes of a large proportion of the youthful and therefore the most susceptible section of the community. Fundamental changes have not been found necessary and none appears to be seriously contemplated in provisional schemes for a comprehensive state medical service; it is anticipated that amalgamation of existing authorities and agencies and extension of more conveniently planned administrative units will solve most of the problems still outstanding.

To what degree either more chance or the maintenance of an adequate dietary and relative freedom from the more immediate evils of war is responsible for this comparatively happy state of affairs, must be left to the compilers of a medical history of the war to assess; at the present time principles and clues may emerge to guide present and future policy and practice. The effects of redistribution of population at different ages into diverse environments and the success or failure of the measures instituted to limit the spread of disease are being closely studied from different points of view.

EPIDEMIOLOGICAL REVIEW: GENERAL

As regards acute infective or epidemic diseases 1942 compares favourably with 1941, which in its turn was favourable when compared with pre-war years regarding all diseases with the important exceptions of cerebrospinal fever, enteric-dysentery-salmonella infections and tuberculosis; all these are well known to be associated with conditions of life incidental to the existence of a state of war. Notifications of the principal diseases in England and Wales are compared below for 1941 and 1942 and for the first quarters of 1942 and 1943.

	1941	1942	INCREASE OR DECREASE	1942 1ST QUARTER	1943 1ST QUARTER	INCREASE OR DECREASE
Measles	405,580	285,300	-	26,535	220,556	+
Scarlet fever	57,982	84,932	+	14,935	26,759	+
Whooping-cough	169,863	65,563	-	18,325	23,005	+
Diphtheria	50,056	42,318	-	11,658	10,799	-
Acute pneumonia	49,547	42,487	-	15,766	18,211	+
Cerebrospinal fever	10,986	6,089	-	2,412	1,287	-
Dysentery	6,485	7,177	+	1,674	1,319	-
Typhoid fever and Paratyphoid fever	4,687	887	-	235	175	-

NOTE.—Cases of measles numbered 204,158 during 1941, 1st quarter.

The favourable trend is seen to be lost respecting measles, whooping-cough and acute pneumonia and regained respecting dysentery, whereas scarlet fever shows an ever increasing momentum. Fortunately the clinical type of scarlet fever remains mild with few complications and exceptionally low fatality rates. In general, measles and whooping-cough also have been mild even amongst the lower age groups upon which incidence has been particularly heavy. The measles figures for the first quarters of the last three years clearly show the biennial periodicity of the disease the rhythm of which was apparently interrupted by the evacuation or dispersal of non-immunes. A similar experience in regard to measles at the same time in the United States of America suggests that this departure from expected behaviour may be more complex and fundamental. Measles may show itself to be as capricious as influenza.

There is a gratifying drop in the incidence of enteric fever and dysentery in the

first quarter of 1943. Cerebrospinal fever continues to decline in incidence, as it did in the fourth year of the war of 1914–18; judging by published reports severity of attack and fatality have also decreased but the number of deaths in 1942 is not yet available. The death rate from certain other infections in the 126 great towns of England and Wales is indicative of severity of attack and fatality over the whole country, and is given for 1941 and 1942 and for the first quarters of 1942 and 1943.

		1941	1942	INCREASE OR DECREASE	1942 1ST QUARTER	1943 1ST QUARTER	INCREASE OR DECREASE
Scarlet fever							
Cases	—	27,062	43,063	+	6,971	14,027	+
Deaths	—	58	55	—	10	26	+
Case fatality	—	0·21	0·13	—	0·01	0·19	+
Whooping-cough							
Cases	—	77,639	34,392	—	9,054	12,478	+
Deaths	—	17,205	468	—	135	171	+
Case fatality	—	1·6	1·4	—	1·5	1·4	—
Diphtheria							
Cases	—	28,229	25,075	—	6,731	6,347	—
Deaths	—	1,530	987	—	337	301	—
Case fatality	—	5·4	3·9	—	5·0	4·7	—
Measles							
Cases	—	147,289	162,010	+	13,997	107,308	+
Deaths	—	503	293	—	33	278	+
Case fatality	—	5·4	0·18	—	0·24	0·26	+
Typhoid fever and Paratyphoid fever							
Cases	—	2,539	343	—	80	52	—
Deaths	—	79	38	—	9	6	—
Case fatality	—	3·1	11·1	+	11·3	11·5	+
Influenza							
Deaths	—	2,993	1,544	—	862	1,149	—

Whereas scarlet fever and measles showed appreciable increase in numbers, the death rate fell in every disease (notably measles and diphtheria) excepting only enteric fever the incidence of which was low but the fatality high owing to the emergence of typhoid fever as the prevailing type. It is permissible to argue that the low fatality of diphtheria is in part attributable to immunization, which very rarely fails to avert a fatal issue even during a period when infection is most virulent.

The epidemiological picture is less favourable in the first quarter of 1943. The only bright spot is a slight improvement in diphtheria. The measles epidemic fell heavily on the great towns but the type, as reflected in the number of deaths, remained mild. The noteworthy characteristic of this disease, in London at least, was the frequent occurrence of suppurative otitis media and mastoiditis; even large doses of the usual sulphonamides failed to influence these complications which were almost invariably due to the haemolytic streptococcus. On the other hand broncho-pneumonia, enteritis and eye complications were infrequent and responded readily to treatment. Since influenza as such is not a notifiable disease the exact prevalence is not known with certainty but a great increase in the number of deaths in the first quarter of 1943, in conjunction with a considerable increase of notifications of acute pneumonia (from 15,766 to 18,211 in England and Wales) suggests that influenza was prevalent and its attack severe.

CURRENT PROBLEMS

Influenza

The behaviour of cerebrospinal fever and of the enteric-dysentery group of infections in the present war has imitated so closely their behaviour during the war of 1914–18 that many observers expect influenza also to follow its 1914–18 pattern. Much knowledge of this disease has been amassed in the inter-war period including identification and cultivation of the causative organism and preparation of vaccines and immune

serums tested under field conditions, but the major problems of influenza continue to baffle investigators.

The latest developments are described in two contributions by the leading research workers in this field of inquiry. C. H. Andrewes (1942) who with his associates, W. Smith and P. P. Laidlaw, discovered in 1933 the causative agent of epidemic influenza (now designated virus A to distinguish it from virus B isolated in America in 1940) discusses the problems of reservoirs of infection in inter-epidemic periods and of change of type, postulating as a working hypothesis a non-virulent basic virus harboured by a number of individuals, especially during periods when winter colds and febrile catarrhs are prevalent. These two affections have been observed to precede outbreaks of influenza and it is probable that by the medium of repeated human passage a non-virulent virus may be raised to the virulence of virus A. This may occur in several foci almost simultaneously. The value of prophylactic measures such as vaccines and the inhalation of atomized serums is assessed and the possible use of antiseptic mists and ultra-violet rays in controlling outbreaks in closed communities is examined. By the light of modern investigation into epidemic influenza F. M. Burnet in collaboration with Ellen Clark (1942) has made a comprehensive survey of epidemic influenza occurring in the last fifty years and especially of his own contributions to the subject. These authors emphasize the complexity of the influenza problem showing (1) that in many typical epidemics failure to isolate virus is more common than success and that during any one outbreak a few only of those affected yield virus and (2) that antibody production may be evoked without overt attack and clinical attack may not be attended by increase of blood antibody. The 1918-19 pandemic received pride of place not only because of its unprecedented prevalence and severity and because its main attack was levelled against young adults but also because it occurred in three successive waves the second of which was the worst. Whether the strain was the same in all three waves and whether virus A was present is not known. The opinion held by Burnet and Clark that the 1918 strain differed from other types chiefly because tissues ordinarily resistant to influenza proved highly vulnerable to it, would if correct portend ill for the future because the vaccines and serums at present available might prove ineffective.

In a recent study Burnet (1942) confirmed that the best antibody response to vaccination with attenuated virus A was obtained from individuals who had some initial antibody content. He applied virus B attenuated by 40 passages in chick embryo allantoic fluid to the nasal passages of volunteers and in these also induced a significant increase in antibody; he suggested that the method might be capable of application in a small group of selected individuals whose resistance to influenza B was low. J. Stokes, Jun and W. Henle (1942) found that formalin-treated virus evoked equally good antibody responses from patients treated by single and by multiple injections. Children who had received this vaccine inhaled atomized allantoic fluid virus through aviation oxygen masks and did not develop typical influenza, although some of them suffered from subclinical attacks. The problem of immunity has been further complicated by the detection in nasal secretions of neutralizing or inhibitory substances which may ward off attack in non-immunes; this may explain in part the apparent vagaries of serum antibody content relative to immunity. The investigators used immune serum locally on the nasal passages of experimental animals and suggested that the method might be applicable to human beings.

Is the balance in favour of a repetition of the 1918 pandemic in the fifth year of the war? In England and Wales influenza A appeared in the first three months of the odd years, 1933, 1935 and so on and particularly extensive epidemics recurred in four-yearly cycles, in 1929, in 1933 and in 1937, but not in 1941. In the even years influenza A has been virtually absent although clinical influenza (probably due to an unidentified strain and provisionally designated Y virus) appeared in some form with variable frequency. Influenza B has not so far been isolated in Great Britain although its presence in the spring of 1943 was proved by the appearance of antibody in a number of individuals suffering from clinical attacks; from tests Andrewes carried out on serums collected in 1939 (C. H. Stuart-Harris, W. Smith and C. H. Andrewes) it appears that this type, milder and less epidemic than influenza A, was also present in that year.

Infective enteritis

Although exact figures are not available for the incidence of infective enteritis

(zymotic enteritis, summer diarrhoea, acute gastro-enteritis) since the present war began, the number of deaths from enteritis or diarrhoeal diseases among children under two years of age is available and provides some indication of the prevalence of these disorders and the severity of their attack. In the five years 1938–42 the annual deaths recorded in England and Wales were 2,324; 2,812; 2,893; 2,985; 2,283 respectively; in the first quarter of 1943 deaths numbered 614 whereas the number for the corresponding quarter of the preceding year was 473. It is suggestive that since the beginning of the war (1942 excepted) infective enteritis has risen steadily more or less at the same rate as the trend of infective diseases involving the respiratory tract, including influenza.

Many circumstances have contributed to the increase in cases of enteritis: the decline in breast-feeding owing to lack of maternal interest or to the work demanded of women combined with a want of appreciation by doctors and nurses of the necessity for natural feeding during at least the first three months of life; the widespread use of ill-adapted and inadequately equipped and staffed day and residential nurseries in which communicable diseases may spread and lead to a fatal attack of gastro-enteritis; and the lack of adequate isolation accommodation for suspected or manifest cases. C. Elaine Field, D. MacCarthy and W. G. Wyllie (1943) recommended the general application of the preventive measures commonly enforced in fever hospitals and in children's hospitals, and outlined schemes of treatment and subsequent feeding. Well-trying measures, including a return to the old-fashioned initial dose of castor oil, formed the basis of these methods. In an outbreak of neonatal diarrhoea in maternity wards J. L. Henderson (1943) used sulphaguanidine in doses of 0.5 gramme (8 grains) every four hours and decided that its therapeutic action saved some lives. The clinical description of the cases indicates that the type of infection in his series was not severe. Other workers have found the drug not to be of any value in this disease.

Succinylsulphathiazole, which has a clear-cut inhibitory action on intestinal coliforms and to a less degree on enterococci, may be of value in some cases in which multiplication and rise of these organisms in the patient's gastro-intestinal tract is pronounced; with its use even in severe cases lactose or glucose is tolerated early but every method may fail which does not eliminate the original focus, which in an appreciable number of cases is found to be the middle ear and mastoid process. Mastoidectomy should be considered in all cases in which patients fail to make satisfactory progress after the initial toxæmia has been combated. In a series of severe cases I found (1943) that succinylsulphathiazole given in doses of 1 gramme (15 grains) four-hourly for from five to seven days produced slightly improved results in the patients' condition; recent (unpublished) experience of the drug in conjunction with bilateral mastoidectomy when indicated has been somewhat more favourable. Preliminary myringotomy is usually performed but almost invariably fails to bring relief as the pus is typically gelatinous and sticky. The pus may be sterile or may contain a variety of respiratory pathogens and occasionally *B. coli*. There is much circumstantial evidence that a virus, possibly allied to influenza virus, may be the primary aetiological agent because high fever without physical signs is the rule in the more malignant attacks and its frequency is highest when febrile catarrhs and influenza are prevalent (not in summer and autumn as formerly). Two American workers, T. G. Folsom and G. M. Lyon (1940), have described an outbreak (involving 15 out of 21 babies of whom 5 died) in a maternity hospital; the outbreak appeared to originate from influenza in one of the mothers and to spread to the infants by direct contact. Citrated influenza-convalescent blood (30 cubic centimetres) injected into each thigh produced immediate good effect with ultimate recovery in three of the worst attacks. The measure is clearly worth further trial.

Enteric, dysenteric and salmonella infections

The great increase in the frequency of ingestion disorders during the war years appears to have been checked; figures for the enteric fevers fell in 1942 to less than one-quarter of those of 1941 and the decrease continued in the first three months of 1943; dysentery, on the other hand, continued to increase in 1942 but decreased somewhat in the first quarter of 1943. Although food poisoning (salmonella infections) has been since 1939 one of the notifiable diseases it does not appear in the weekly summary and therefore no official figures are available. According to published accounts and reports it remains a serious menace although like dysentery it has probably declined slightly.

Enteric fevers.—Second only in importance to detection and elimination of the source of infection in an outbreak is the search for carriers or missed ambulant cases. Highly selective media such as those of Wilson and Blair now make this task easy and exact but occasional intermittent excretors require repeated examinations over weeks or months before they can be pronounced negative. The carrier problem continues to defeat intense study; iodophenolphthalein has been found a little restricted in its application to biliary carriers because in chronic cases the drug too often either failed to be secreted in sufficient concentration in the gall-bladder or did not reach the infected biliary passages; the purely intestinal carrier has not been found to respond to sulphaguanidine (L. Oppen and Virginia Hale, 1942; T. F. McN. Scott, P. B. Beeson and W. L. Hawley, 1943) nor to mepacrine (Medical Research Council, 1942¹). Succinylsulphathiazole has not yet received an adequate trial; L. A. Rantz and W. M. M. Kirby (1942) found it to be effective when used in the treatment of dysentery but not in the treatment of typhoid carriers.

Dysentery.—Reports continue to be favourable respecting the use of sulphaguanidine in cases of both Flexner and Shiga forms of dysentery but a positive verdict cannot be given regarding Sonne dysentery. Two important papers each dealt with a long series of cases occurring among troops in the Middle East. N. H. Fairley (1942) found Shiga antitoxin disappointing, mitigation of toxæmia being only temporary; sulphaguanidine, if given early in large doses, produced rapid resolution and elimination of organisms. Sulphasuxidine (succinylsulphathiazole) and sulphamethazine were also tried and gave promising results. Acute and chronic cases of Flexner and Shiga dysentery comprised A. E. Brewer's series (1943). In acute cases patients naturally responded better even with a lower dosage. In chronic cases patients received a preliminary course of colonic lavage and progress was measured from time to time by sigmoidoscopic examinations; the average total dose of sulphaguanidine was 140–160 grammes which caused toxic symptoms in nearly 20 per cent of the cases. The findings at Oxford (Medical Research Council, 1942²) suggest that current criteria of freedom from infection are not sufficiently strict, particularly regarding patients in institutions.

Food poisoning.—It may be difficult to distinguish clinically between food poisoning and dysentery, especially in young children. W. Savage in a survey (1942) made practical suggestions for the detection and control of outbreaks. Three types of food poisoning are recognized. (1) *Salmonella*, which causes about 70 per cent of the outbreaks in Great Britain (case mortality 1–2 per cent); (2) toxin outbreaks, rare, chiefly staphylococcal (case mortality practically nil); (3) botulism, very rare, only three small outbreaks recorded in Great Britain (case mortality 60–70 per cent); but suitably conditioned organisms such as *B. coli* and *B. proteus* may alter food sufficiently to cause symptoms of poisoning. Unlike enteric organisms which invade the blood stream, food poisoning organisms remain localized and set up an acute gastro-enteritis; in young children bacteraemia may occur producing a picture indistinguishable from that of enteric fever. The agglutination test is applicable in the larger number of cases and may permit an accurate retrospective diagnosis should the faeces be found negative before the patient comes under observation. With more recent methods of cultivation these organisms have been found to persist for much longer periods than was formerly thought to be the case. *Salmonella* infections do not generally show any response to sulphonamide therapy either in the form of modification of the disease or in shortening of the period of infectivity.

Smallpox

The outbreak in Glasgow of malignant smallpox (*variola major*) which lasted from the 29th of May to the 31st of July, 1942 combined with the subsequent spread of the disease over a large part of Scotland weakened considerably the confidence of public health and port authorities and of the general population in the adequacy of recognized measures of smallpox control. Even faith in the efficacy of vaccination as ordinarily practised has been disturbed by some experiences. From their observations A. MacGregor and R. J. Peters (1942) have concluded that to ensure complete safety, vaccination and revaccination if necessary should be performed before exposure; to this end all travellers from infected ports should be vaccinated if they have not been successfully vaccinated within the previous few years—five years is usually regarded as safe.

Despite careful investigation, according to I. N. Sutherland (1943) no connexion

could be traced between the Glasgow outbreak of smallpox (11 ship cases, 21 untraceable cases, 4 contacts) and outbreaks in the two subsequent foci in Scotland, Fife (3 untraceable, 26 contacts) and Edinburgh (13 untraceable, 16 cases in a convalescent home, the only connexion being laundry and ambulances, 7 contacts). On the other hand there were several instances in which presumed infectious persons in the prodromal or early eruptive stages failed to transmit the disease even to unvaccinated close contacts. Failure to control the outbreak by selective vaccination, that is of known contacts, made necessary resort to general vaccination campaigns in all three areas; these were effective in stamping out the disease. It was considered that but for the effect of vaccination the severe type of smallpox prevailing would have caused a higher case mortality than that which occurred, 24 per cent. Rather unexpectedly individuals who had been vaccinated in infancy appeared to have a better immunity than those vaccinated once at a later period in life; there were a few instances of patients successfully vaccinated who did not escape attack, even as long as ten days after a good 'take'. These findings are at variance with the experience of most authorities. Some use was made of the Gordon test in doubtful cases but probably some were erroneously accepted as smallpox and others were missed. Failure to make chicken-pox notifiable in the areas and at the periods in question may have been responsible for some of the missed and possibly also for some of the untraceable cases.

The incidence of severe febrile reactions, vaccinal eruptions and post-vaccinal encephalitis was high especially in some districts, associated perhaps with certain batches of lymph. Government lymph mainly was employed. The encephalitis cases were distributed thus, deaths in brackets: Glasgow 7 (2); Fife 9 (4), Edinburgh 11 (2); Lothians 7 (4). This high incidence sharply contrasts with the 1921 Glasgow epidemic when nearly a quarter of a million vaccinations were performed without increase in deaths from encephalitis. It would appear that the strain used in 1942 in the preparation of the lymph had exceptionally high encephalitogenic characteristics but nevertheless, in accordance with usual experience, infants remained free from this dreaded complication. Of the seven Glasgow cases six occurred in previously unvaccinated children between the ages of two and sixteen years, reinforcing the argument in favour of vaccination in infancy.

Infective jaundice (toxic hepatitis)

A few outbreaks of jaundice were encountered in the Forces during the war of 1914–1918 but Great Britain was free from the disease in epidemic form until it reappeared amongst the troops in France in 1939; several outbreaks have since been reported in the Forces and in the civilian population both in Allied and in enemy-occupied countries. Certain characteristics, notably a short incubation period (from twenty to thirty-two days) and a relatively benign course distinguish this disease (generally assumed to be due to a filtrable virus) from toxic hepatitis following inoculation of human serum or blood, in which the incubation period may range from one to three months or longer with severe focal liver damage and death in an appreciable percentage of cases. In a memorandum by the medical officers of the Ministry of Health (1943) the clinical and epidemiological characters of the disease are fully detailed but the compilers were unable to decide whether the morbid processes were a result of toxic, allergic or viral activity. Most workers accept the last assumption in practice at least and consider it advisable to maintain contact with blood donors for one month lest jaundice should ensue.

The experience of some observers that toxic hepatitis ensued after inoculation of yellow fever vaccine supports the view that the virus of infective jaundice was the contaminant. When G. M. Findlay and F. O. MacCallum (1937) and G. M. Findlay, F. O. MacCallum and F. Murgatroyd (1939) encountered jaundice after their inoculations they decided to use fresh cultures and human serum heated for thirty minutes at 56° C.; thereafter no further cases appeared. The disease appeared in 1942 among American troops, killing sixty-two patients out of 28,585 (case mortality 0·02 per cent). Efforts to transmit the disease to animals were unsuccessful but it has been proved that yellow fever virus is not the cause. The American army vaccine is now made with chick embryo suspension in distilled water without addition of human serum (Circular Letter No. 95, 1942). The subject has also been dealt with by the War Office (1942).

PROPHYLAXIS

(1) General measures (non-specific)

No new principle has come to light during the year in connexion with prevention or spread of infection. Measures such as oiling of floors (with spindle oil) and of fabrics (with 3 per cent technical white oil in an emulsifying agent) to allay germ-bearing dust are well known but only the first expedient is being widely employed; the practical difficulties of the second have not yet been overcome. Sterilization of atmospheres by chemical mists (resorcinol, hypochlorite salts) has not been extensively attempted on account of inherent difficulties; propylene glycol is considered by some American workers to be the ideal bactericidal vapour but this substance is not available for use in Great Britain. For the same reason the use of ultra-violet rays is not likely to be established in Great Britain until after the war. Considerable advances have been made in the United States of America and the subject of atmospheric sterilization has been given the status of an applied science. The newer methods (especially irradiation, both ceiling and screen types) have been extensively used there in hospital wards and in schoolrooms. The theoretical and practical aspects are comprehensively investigated and described in a volume entitled *Aerobiology* (1942).

(2) Recent advances in active immunization

The conclusion arrived at by Downie and his associates (see Medical Progress (Critical Survey Section) 1943, p. 56) that combined passive and active immunization (indicated in special circumstances) is an efficient and practicable procedure has been confirmed by J. J. Phair (1942¹) in experiments on guinea-pigs; he also found that a non-virulent strain of *Corynebacterium diphtheriae* was effective in providing the required secondary or 'boosting' stimulus. In a further study (1942²) the same author, having obtained success in thirty-three out of thirty-four cases, recommended instillation of glycerin-toxoid mixtures into each nostril of adults who had been sensitized but not completely immunized by a previous primary stimulus. This method, originally practised by Jensen, has received little attention in Great Britain where the relatively bland toxoid-antitoxin floccules preparation is generally used in highly sensitive usually adult individuals.

There is now general agreement that alum precipitated toxoid, in doses of 0.2 cubic centimetre (50 L₁ units per cubic centimetre) and 0.5 cubic centimetre given intramuscularly at a four-weekly interval, provides adequate immunity responses in numbers ranging from 95 to 100 per cent as determined by the Schick test. Direct titrations however make clear that this test is apt to show a considerable margin of error explaining the occasional appearance of clinical diphtheria in negative reactors. From his experience in a London borough, V. Freeman (1942) concluded that a preliminary Schick test is desirable in children over ten years of age, since one-third of those tested over that age are negative and do not require inoculation; negative reactors form on the whole a sensitive group, prone to untoward reactions from inoculation. A post-immunization test should always be made if for no purpose other than to assess the efficacy of different antigens and batches. Contrary to general experience and to the official recommendation (Ministry of Health; 1942) Freeman found injections made two-weekly and four-weekly to be almost equally effective and urged the former time interval as more convenient for administrative reasons. Combination of antigens continues to give promising results. Pearl Kendrick (1942) found that alum-treated pertussis vaccine gave results slightly superior to those of standard vaccine, the results were still better if the first-named vaccine were combined with diphtheria toxoid, the subsequent attack rate being 0.7 per 100 as compared with 1.6 in the case of standard vaccine and 10.9 in the control (uninoculated) group. J. J. Miller, Jun. and T. M. Saito (1942) used pertussis vaccine combined with diphtheria and tetanus toxoids. The responses were satisfactory except against tetanus and a third injection (without diphtheria toxoid) was recommended to be given three to four months later. American army authorities give a dose of tetanus toxoid immediately after injury whereas British practice remains as before, namely 3,000 units of antitoxin or more, depending on the lapse of time between injury and administration. A manual of immunization entitled *Preventive Inoculation*, by W. P. Phillips and C. W. Anderson (1942), epitomizes current practice.

(3) Administrative procedures: modifications

There has been a tendency in the last two decades to relax the strict rules of quarantine in the home, in schools and even in hospitals. It is realized more and more that the loss of school attendance or of working hours is rarely compensated for by any advantages which might be gained from strict enforcement of isolation and quarantine; accordingly a system of surveillance of immediate contacts is being substituted, combined with detection of carriers and protection of presumed susceptibles according to circumstances. The method may fail on occasion but many potentially dangerous epidemics are checked almost daily by it. Official endorsement of this line of action is incorporated in a memorandum issued by the Ministry of Health and Board of Education jointly (1942), dealing with school closure. M. Mitman (1943) discussed at length the difficulties relevant to hospital practice, he concluded that every outbreak should be dealt with according to the particular circumstances, of which infectivity of the disease, severity of attack and proportion of non-immunes at risk are the most important.

TREATMENT

Recent developments

Except in the treatment of diphtheria, sulphonamides are rapidly replacing serums; considerations of supply and cost still prevent a final decision on the comparative merits of the two favourites, sulphathiazole and sulphadiazine, for systemic infections. Neither is suitable for local application, although the micro-crystalline form of sulphathiazole has been found superior to other preparations for local use especially for skin infections such as impetigo. Speaking generally, the use of sulphonamides in wounds and on open surfaces has failed to justify the high hopes raised by their early promise. Two substances, penicillin (M. E. Florey and H. W. Florey, 1943) and propamidine (W. R. Thrower and F. C. O. Valentine, 1943), may supplant sulphonamides for local application; moreover penicillin undoubtedly has been proved to possess great therapeutic potentialities, especially for staphylococcal invasions, even in cases in which adequate sulphonamide therapy had failed. Technical difficulties have hitherto stood in the way of preparing adequate amounts of this substance for general use but at least one British firm specializing in biological products is manufacturing penicillin on a commercial scale. The results of its wider use in therapeutics are eagerly awaited.

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DISEASES OF THE LUNGS

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ANATOMY OF THE LUNGS AND BRONCHI

Bronchography

Recent advances in applied anatomy.—For many years the anatomy of the lungs, and especially of the bronchial tree as a whole, was a subject of but little research, and traditional descriptions of the lobes of the lungs and the distribution of the various subdivisions of main bronchi remained unaltered. With the advent of modern thoracic surgery came an increasing recognition of the importance of applied anatomy in regard both to the thoracic viscera in general, and in particular to the lobar subdivisions of the lungs and the distribution of the corresponding portions of the bronchial tree. The contributions made in the last few years to the literature of this subject represent one of the most notable examples of the ideal combination of academic and practical studies—a combination that may fairly be said to have been responsible in no small degree for the successful achievements in the surgical treatment of many diseases of the chest hitherto regarded as incurable.

Terminology.—In an article published in 1934 on postural treatment of bronchiectasis, the late H. P. Nelson, who had worked for some time on the anatomy of the respiratory organs considered in its application to the surgery of the chest, reproduced some novel diagrams of the lungs. He regarded each of these organs in terms of four principal areas, namely an upper zone, a middle (ventral) zone, a dorsal zone and a lower zone. He also gave a practical terminology of the distribution of the bronchial divisions in relation to these zones, which constituted the foundation upon which are based most of the present-day readings of radiological pictures of the chest so far as concerns the localization of lesions for which surgical intervention is contemplated. His diagrams have been adopted as representing a practical improvement on the usual anatomical concepts, and this method of regarding the lungs and bronchi has been rendered still clearer by an admirable recent contribution on the anatomy of the bronchial tree by A. F. Foster-Carter (1942). This contains a full historical survey of the subject, with diagrams of the tree and of the broncho-pulmonary segments according to various authors. The description given by him of the bronchial tree is based upon a study of about 200 bronchograms, as well as upon dissections, inflation preparations and actual casts. This paper is perhaps the best example known of a method of description now generally in vogue among those who are mainly interested in diseases of the chest, and to whom anatomical considerations are essentially a matter of practical application. It may well be taken as a standard.

Bronchography.—R. Adams and L. F. Davenport (1942), in a paper on the technique of bronchography, have suggested a terminology of the bronchial tree designed to meet the needs of radiologists, physicians, surgeons and bronchoscopists who work in teams and for whom, in the authors' view, an adequate practical nomenclature is yet lacking. Apart from slight differences in detail, their description corresponds more or less to those already mentioned. Some useful diagrams are appended, illustrating various positions to be adopted by the patient for whom a bronchogram is desired. A shorter paper is supplied by F. D. Hart (1942) which, although it lacks the detail and the illustrations given in the two former contributions, has the merit of brevity and simplicity and is perhaps more useful as a preliminary to these.

Pulmonary collapse after injection of iodized oil.—Germane to the study of the above communications are the results of observations by F. J. S. Gowar and J. R. Gilmour (1941), on the changes in the lung occurring after injections of iodized oil into the trachea. These changes are of importance, especially on account of the light they throw upon the question of the relation of pulmonary collapse to the presence of oil in the divisions of the bronchi. Evidence is adduced to show that, when collapse of the lung occurs in these circumstances, it is due to a cause other than the injection of oil. Gowar and Gilmour conclude, however, that the introduction of iodized oil into the

air passages may influence the occurrence of massive pulmonary collapse owing to its mechanical effect in predisposing to bronchial obstruction, and that collapse effects are due to this, rather than to any histological changes in the lung caused by the presence of the oil.

BRONCHIAL ADENOMA

Symptoms and clinical course

The classical description, in 1932, by H. Wessler and C. B. Rabin of adenoma of the bronchus necessitated the revision of not a few histological reports in cases which had been recorded as examples of primary bronchial carcinoma. Since the publication of the above paper in which seventeen benign bronchial tumours were described, twelve of them being adenomas, numerous other accounts have appeared and this type of growth is now well recognized. The summary given in 1941 by A. F. Foster-Carter provides an excellent account of the literature up to that date. In the article the author reviews the records of about 100 cases already reported, and adds detailed observations on twenty-two cases investigated at the Brompton Hospital, London, of which the notes are appended. The thesis is extremely well illustrated and deserves the closest study. The radiographs and microphotographs are well reproduced and are really instructive. The symptoms of the condition are described as being divisible into two main groups, namely those directly due to the presence of the tumour, for example haemoptysis and cough, and those resulting from the bronchial obstruction. Dyspnoea is noted as a conspicuous symptom in 31 per cent of all cases. The average duration of the disease, since the onset, in fifteen of the Brompton Hospital patients who had survived (seven of them died) was ten years.

BRONCHIECTASIS

New concepts on pathogenesis

Radiological observations.—The steady progress of radiology and the ever increasing improvement being made in radiological technique are altering to a considerable extent the older conceptions of bronchiectasis, not only in regard to its incidence and manifestations, but also in regard to its pathogenesis. Since the introduction of bronchography, whereby it is possible to obtain a fairly accurate picture of the bronchial tree as a whole, the notion of bronchiectasis as an anatomical state rather than as a clinical entity has gradually gained ground. This has modified in no small degree the traditional teaching in regard to this disease, which was based largely on statistics drawn almost entirely from records of advanced cases in which the effects of infection were seen at their maximum. Such records took little or no account of the lesser degrees of bronchiectasis, or of the occurrence of relatively uninfected cases which, in days when radiography was yet in an embryonic state, gave practically no clinical evidence of the existence of any material structural changes in the respiratory tract.

Pulmonary collapse.—The publication of an original paper on atelectatic bronchiectasis by A. J. S. Pinchin and H. V. Morlock (1930), calling special attention to the phenomenon of the basal triangular shadow, in connexion with which the authors regarded bronchiectasis as the most commonly associated lesion, was probably the first real stimulus to searching enquiries into the significance of pulmonary collapse as an aetiological factor in bronchial dilatation. J. V. Sparks (1931), P. Kerley (1932), R. W. B. Ellis (1933), L. Findlay (1935) and others have made further more detailed observations. When F. P. L. Lander and M. Davidson (1938¹) maintained that collapse was the chief and, in fact, the sole factor in the production of bronchiectasis, and dissociated themselves from the long-accepted view of infection as a primary cause, no little controversy arose and, although there may now be said to be two schools of thought upon this question, the matter can hardly yet be regarded as decisively settled.

Bronchial dilatation and infection.—An extremely careful and detailed investigation into the whole subject has been conducted by A. G. Ogilvie (1941), in which the problem has been given special consideration. This author's observations on the histological aspects of bronchiectasis are directly at variance with those of F. P. L. Lander and M. Davidson (1938²), and are supported by numerous excellent microphotographs. Ogilvie concludes from the available evidence that the bronchial wall is often weakened by the action of infections which, in his view, are responsible for the occurrence of actual destruction and for its subsequent extension. He considers, moreover, that bronchial dilatation may be temporary or permanent, the former effect always being due to

pulmonary collapse, but the latter being the resultant of many factors, of which he regards infection of the bronchial wall as the most important. Ogilvie's thesis does not deal with the treatment of bronchiectasis; as a study of the aetiology, morbid anatomy and histology, radiological and clinical features, classification and natural history of the disease, it is one of the most comprehensive and accurate research studies that have appeared in the literature, and is a valuable stimulus to further enquiry on similar lines.

Treatment

The early diagnosis of the condition by radiographical means has undoubtedly permitted a considerable improvement in existing methods of treatment, and has given to the thoracic surgeon both impetus and opportunity to deal radically with numbers of patients who, not many years ago, would have been abandoned to a life of chronic invalidism, tempered at best by the palliation afforded by postural drainage and by general medical measures which, although successful in some instances, were often lamentably disappointing in others. At the same time it must be said that the more extended observation of patients which radiological research has made possible, as well as the records of large numbers of patients kept under observation subsequent to primary treatment, have forced us to revise to some extent earlier opinions formed concerning the prognosis of bronchiectasis as a whole. Personally I yield to no one in appreciation of the debt which many of these patients owe to the achievements of major thoracic surgery, but I would say at the same time that the most recent studies of the natural history of bronchiectasis compel a careful and critical selection of patients for operative treatment and recognition of the fact that there are not a few patients with unilateral lesions for whom radical extirpation of the bronchiectatic area, even in a good-risk case, is not invariably the treatment of choice.

Bronchiectasis in the Forces.—L. C. Martin and F. R. Berridge (1942) report twenty-five cases of bronchiectasis without disability. One of the authors' main purposes is to call attention to examples of this condition among serving soldiers (most of whom were graded A1), and to show how even extensive bilateral disease can occur in men of healthy appearance with little or no incapacity to continue their usual duties.

MASS RADIOGRAPHY

Results of recent investigations

Incidence of pulmonary tuberculosis.—The importance of mass radiography has received increased attention within the past few years and it is becoming more than ever apparent that what this method of investigation provides is of incalculable value to preventive medicine. In 1942 W. E. Lloyd gave a comprehensive summary of the literature up to date, with a *résumé* of essential points in the technique of the method and of the statistical results of examination of large numbers of individuals. A few of these results may be quoted by way of illustration. In S. F. Dudley's series, 18,751 miniature film records were made with the special apparatus; of the individuals thus examined 672 had full-sized films taken by the ordinary method, and sixty-nine patients were seen in whom pulmonary tuberculosis was suspected. Of these, forty-seven were found, on complete investigation, to have active lesions. The incidence of active tuberculosis thus discovered by the mass examination of a very large number of men in the Royal Navy, who were ostensibly fit and without manifest symptoms of disease, was 0.25 per cent (1941). The other two outstanding examples of investigation by mass radiography is that of D. Galbraith (1941) who, in a series of more than 100,000 recruits in the Australian Military Forces, found 1.04 per cent with active or latent pulmonary tuberculosis, the lesions being active in 0.56 per cent of the total number, and that of E. L. Cooper (1940) who found 109 cases of active tuberculosis in an investigation of 22,000 recruits of the second Australian Imperial Force, that is 0.49 per cent of the total number.

Use in industrial medicine.—The details in regard to important points in technique are discussed in the three papers referred to above and in many others to which the references are given in Lloyd's survey. Sparks (1941) has also contributed valuable suggestions relating to some of the practical problems which the adoption of a scheme for mass miniature radiography on a national scale would inevitably entail. Of special interest and significance is his statement that Messrs. Phillips & Co., of Eindhoven, examined in the course of seven years 100,000 employees and their relatives, and that, during this period, the annual sick leave directly resulting from tuberculosis

among the firm's employees was diminished by as much as 71 per cent, for an expenditure of 88,000 guilden (about £7,500), 252,000 guilden (about £22,000) was saved in expenses for sick pay, medical treatment, sanatorium benefit and pensions. Some useful remarks on technique and on the viewing of films are added, with instructive comparative reports of miniature and full-sized negatives.

There can be little doubt in the mind of any impartial student of public health who is acquainted with modern views on the pathogenesis of adult human pulmonary tuberculosis, and with the vital importance of X-ray examination as the sole means of detecting the early granuloma in its symptomless stage, that mass radiography is far more than ancillary to clinical medicine. It is obvious that, considered from the standpoint of the ideal, it should be accepted in the near future as an integral part of any scheme of national health insurance that is to be worthy of the name. We are fully cognizant of the numerous difficulties—political, social and economic—that its introduction on so large a scale will necessarily present, to say nothing of the possible problems of professional etiquette also which may arise in case of the voluntary submission of large numbers of workers to such a method of examination. It is necessary to draw attention to the possibility of difficulties such as these without any attempt to underestimate them, not indeed by way of discouragement but in order that they may be faced and overcome.

It is distressing, in view of the vital information that has come to light as the result of all the pioneer work on a subject so closely related to the prevention of what has been described as one of our great national scourges, that there still should be so many clinicians holding posts of responsibility who fail to recognize the existence of the symptomless lesions of pulmonary tuberculosis in adolescents or in young adults, and who still endeavour to teach, in the face of conclusive disproof, that such lesions can be detected by careful clinical examination. The observations of workers who have had to deal with increase of tuberculosis since the outbreak of the present war are already providing the most cogent evidence, not only of the value of mass radiography, but also of the obvious need for its universal adoption.

PRIMARY CARCINOMA OF THE BRONCHUS

Incidence, diagnosis and treatment

The awakening of the medical profession to the apparent increase in the incidence of cancer of the lung seems to have coincided more or less with the rebirth of thoracic surgery after the war of 1914-18. Although improved knowledge of the clinical and radiological features of primary bronchial carcinoma and the increased facilities for earlier diagnosis afforded by bronchoscopy have not been accompanied by a corresponding degree of success in treatment, there has been, nevertheless, very positive progress and the condition, while it is always a grave one, is not by any means always hopeless.

Total pneumonectomy.—It is now generally appreciated by all who are really familiar with present-day methods of treatment that the only procedure that offers any real hope of genuine cure is total pneumonectomy. One of the most comprehensive accounts of the disease is that given by A. Ochsner and M. DeBakey (1941). These authors report 116 cases in which total pneumonectomy was performed for malignant disease of the lung. Out of ninety-four cases in which the results are recorded, thirty-eight patients (40.5 per cent) recovered, and fifty-six (59.5 per cent) died. There is not, so far, any collection of data which would afford reliable estimates of the survival chances in the patients who are still alive. The figures quoted are sufficient to indicate the possible benefits now offered by total pneumonectomy in comparison with the results of treatment ten years ago; they may be said to justify the hope and faith with which this procedure has been approached by thoracic surgeons.

Irradiation.—In inoperable cases there remain two main forms of treatment, namely the use of radium and of deep X-ray therapy. The results of radium therapy appear to me to have been somewhat disappointing on the whole, although undoubtedly benefit is obtained in some cases. The best available accounts are those supplied by F. C. Ormerod (1933), (1937), (1941), who has recorded observations on the radon treatment of at least 133 patients with bronchial carcinoma. He gives convincing evidence that in all cases of this disease the expectation of life was advanced from 3-5 months to 7-8 months, and he adds important information about the relief of symptoms in individual cases. As regards deep X-ray therapy, there is still some difference of

opinion about its value, even as a palliative measure. Until the present time it has been difficult to assess its value, mainly owing to the lack of sufficient reliable statistics; and opinions, favourable or otherwise, seem to have been based chiefly on clinical impressions which necessarily vary with individual experience and which, in the absence of very careful scientific control, are notoriously apt to be fallacious. My own impressions, gained from personal experience, have always been in favour of a trial of deep irradiation in cases in which radical surgery was not feasible. A paper by W. V. Tenzel (1941) is valuable for its analysis of 192 treated and untreated subjects with primary lung cancer examined at necropsy at the Montefiore Hospital, New York. A comparison of the results in sixty-eight patients treated by irradiation with the phenomena observed in 121 untreated patients showed an average survival period (from the onset of symptoms until death) of fifteen months in the former group as against ten months in the latter. The author also notes a positive and progressive increase in the survival period in cases in which the 'tumour dose' had been increased from 1,000 roentgens to 5,000 or 6,000 roentgens.

PULMONARY TUBERCULOSIS

Recent observations

Pathogenesis.—The present-day conception of pulmonary tuberculosis differs widely from that entertained at the beginning of the century. Since the publication in 1924 of K. A. L. Aschoff's famous lecture on the pathogenesis of adult human pulmonary consumption, ideas have been undergoing constant change; in regard to the mechanism of the disease much has been elucidated which must, however, still be regarded as attractive hypothesis rather than as scientifically established fact. A helpful summary of modern views has been given by R. C. Wingfield (1942) who discusses the bronchogenic and the haematogenous origins of the pulmonary lesions and the closely related question of exogenous superinfection and endogenous reinfection. His paper is short and is written on lines with which readers of his former monograph (1937) are familiar. Apart from the interest which they evoke in the pathogenesis of the disease, Wingfield's observations are of great practical significance in so far as they emphasize the importance of the 'silent lesion', already referred to above.

Healing of cavities.—Further light has been thrown on the behaviour of cavities by W. Pagel and F. A. H. Simmonds (1942), whose observations on the mechanism of closure and healing are of considerable interest. They refer in this connexion especially to the beneficial effects of caseous bronchitis in so far as it may, and often does, cause occlusion and subsequent healing of the vomica although, if the occlusion be only partial, it may allow air to enter but not to leave, and may thus lead to the formation of a distention cavity, with the possibility of rupture and infection of the pleural space.

Artificial pneumothorax treatment.—F. A. H. Simmonds (1941) has drawn attention to the significance of cavities in connexion with artificial pneumothorax therapy, and has pointed out that effusion occurring during the course of such treatment may be a complication of persistent cavitation—effusions which are due simply to a pneumonolysis, in the absence of cavity, being usually transient and seldom serious. In his experience perforation and pleural effusion are uncommon when the lung cavities are closed, and occur often if the cavities are larger after divisions of adhesions, a phenomenon which is occasionally observed. Another useful publication which has a bearing on this point is that of B. R. Clarke and S. L. W. Erskine (1940), whose research comprises the subsequent observation of artificial pneumothorax cases in patients up to thirteen years, with reference to the mortality rate. The authors provide some striking evidence of the failure, in more than half the number of cases reviewed, to attain a satisfactory collapse of the lung, they conclude that the most important cause of such failure is delay in beginning the collapse therapy. A more recent review, which also deserves study, is that of H. G. Whitehead (1941), who reports on 172 patients with pulmonary tuberculosis who have undergone pneumothorax treatment; he gives a good practical summary of the various factors which influence the ultimate results of such therapy.

The erythrocyte sedimentation rate

Clinical use in prognosis.—Much has been written on this subject, but so far a general consensus of opinion has not been reached concerning its value in pulmonary tuberculosis apart from the belief that it possesses a certain prognostic significance, which corresponds more or less to that of the clinical evidence. G. Berg (1942) has investigated nearly 2,500 cases of open tubercular disease, and concludes that the erythrocyte

sedimentation rate, considered in conjunction with the bacteriological examination of the sputum, does give early information regarding the ultimate outlook. In his series the death rate after three, five and ten years was considerably higher in patients with a high sedimentation rate (over 40 millimetres Westergren) than in those with a low rate (from 1–10 millimetres Westergren). Another interesting survey comes from E. Lewis-Fanning and M. Myers (1942) who made a series of estimations in all patients admitted to the Brompton Hospital Sanatorium, Frimley, during the three years 1936–9. They regarded the test as being only of very limited value as an index of progress in individual cases, and not an improvement on the usual methods of examination. Their investigations did, however, lead them to think that, in regard to the more remote as distinct from the immediate outlook, there was some likelihood of the former being better in those patients whose erythrocyte sedimentation rate fell during sanatorium treatment than in those in whom it rose or failed to approach more nearly to normal levels.

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MENTAL DISEASES

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LEUCOTOMY

E. Moniz's now famous operation (1936), the first surgical attack on the brain in mental disease, is being experimented with to an increasing extent in English-speaking countries. Slight variations in technique have appeared, but the essence of the procedure, the severance of more or less of the fronto-thalamic association tracts in the frontal lobes on each side of the midline, remains the same.

Technique

W. Freeman (1939) makes a lateral approach with a trephine opening in the temporal region on each side, the opening being made 6 centimetres above the zygoma and 3 centimetres behind the orbital margin. He makes four successive cuts in a vertical plane, two on each side. In cooperative patients this is done under a local anaesthetic; with the last only of these cuts, according to W. Freeman and J. W. Watts's observations (1942), does the patient become confused, as if the maintenance of complete mental function depended upon a minority of the total number of fibres being left in action. J. S. McGregor and J. R. Crumbie (1942) use the same approach, but instead of a nasal septum elevator they use an expansible leucotome, which can be adjusted after insertion to give a cutting edge which can be rotated through a diameter of 2.5 centimetres. The class of case in which successful results have been claimed is that which comprises the chronically agitated violent schizophrenics (E. A. Strecker, H. D. Palmer and F. C. Grant, 1942), involutional melancholics (Strecker, Palmer and Grant; Freeman and Watts; E. L. Hutton, 1943; and G. W. T. H. Fleming and W. McKissock, 1943) and chronic depressive psychotics with obsessions (Freeman and Watts). Improvement has been recorded also, for example, in hypochondriacal depression and hebephrenic and paranoid schizophrenia (Hutton).

Limited scope of treatment

The treatment, because of its finality and of the fact that in a few cases it results in an undoubted deterioration of the personality and even in dementia, and because of the risk to life from haemorrhage and of the possible complications (chiefly epileptic fits, aphasia and incontinence of urine), is justifiable only as a last resort. It does not seem justifiable to perform the operation on a melancholic on whom electrical convulsion treatment has not been tried first unless there is some very clear contra-indication to the latter. Some observers have reported totally disappointing results. Strecker and his co-workers consider that a syndrome composed of fear, anxiety, actual mental suffering and aggressive violence is a better criterion for suitability than a diagnostic label.

Effects of leucotomy

As regards after-effects, apart from symptomatic improvement, there has been recorded a return of faculties considered lost, for example artistic capacity, a return of energy and interest, greatly increased appetite and a gain in weight, and even an improvement in the pre-psychotic personality. Thus Strecker, Palmer and Grant record of one patient that she exhibited resourcefulness and common sense to a degree which she had never previously possessed; although on the debit side there is apt to be a shallowness of feeling, a loss of tactfulness and a tendency to live at a simpler level of interest. Freeman and Watts believe that the fundamental alteration is a diminution of self-consciousness. In the violently disturbed patients the gain consists at least of their being made an easier problem of management. In melancholics the apprehension and anxiety disappear. Hallucinatory and other psychotic ideas may remain, but the patient is no longer disturbed by them. It is as if a 'pathological point' in the cortex had been screened off from its mental connexions, and like I. P. Pavlov we are reminded of the naïve-looking hypothesis of Clérambault that hallucinations arise from some focus of irritation in the brain substance and are at first disregarded (1941). After leucotomy there is not usually any measurable loss of intelligence, but

there may be less initiative. Hutton believes that 'reproductive memory is replaced by associative memory so that the patients live in a 'perpetual present' (E. L. Hutton, 1942).

SHOCK THERAPY

Types of treatment

The precise value of shock therapy continues to be a matter of discussion. As regards electrical convulsion therapy, its value in involutional depressions cannot be questioned. Thus an estimate of 70 per cent of rapid recoveries in this group is on the low side compared with general experience (B. C. Quick, 1942). With depressions in earlier life it is successful much oftener than not, but there are some risks in this group of early relapse and replacement by manic episodes and possibly of facilitation of recurrence later on. Relapse can often be cleared up by a further course. There is an unfortunate tendency to apply it very early to patients with relatively mild depressions who may recover fairly soon in any case. It is no light matter to apply treatment of this sort to any person who afterwards may have to earn his living by his brain. It is usually stated that the obvious memory defect which occurs after treatment clears up in six weeks or a little more, but in some cases a degree of memory defect persists much longer than that, although it does not necessarily involve current memory, but only the memory of episodes before the illness.

In schizophrenics electrical convulsion treatment has on the whole proved disappointing so far as ultimate results are concerned, although it is well known that it was for such conditions that it was originally introduced. A. E. Bennett (1942) is one of those who point out that the results are inferior to those obtained with insulin, as far as can be judged, and possibly no better in the long run than non-shock methods. H. A. Palmer (1942) treated ninety patients with either insulin or cardiazol (leptazol) or electrical convulsion treatment, choosing the method at random in each case, and concluded that insulin and convulsant methods gave about equally good results, with a slight superiority in favour of the latter. His insulin treatment was brief by the usual standards (twenty comas) and it is doubtful if his group was so constituted as to give a satisfactory basis for judgment. It seems on the whole that convulsion therapy in schizophrenics is not of much permanent value although it can certainly produce temporary improvement, even in hebephrenic types, in early cases.

Insulin.—Insulin remains the method of choice among the shock forms of treatment in schizophrenics of any type, but whether it does more than shorten the attack in cases which would otherwise have had a favourable outcome is not yet wholly clear. Even an alleviation of such an illness is, however, a considerable advantage. There is some evidence that the satisfactory results may be related to the skill with which treatment, especially insulin treatment, is conducted. Thus T. D. Rivers and E. D. Bond (1941) asserted that while 79 per cent treated within the first year of illness either recovered or were much improved, the rate was only 46 per cent in a similar group of patients treated by inexperienced therapists. C. O. Cheney and P. H. Drewry, Jun.'s observations in 1938 should be remembered, in which they demonstrated the effect of a well conducted therapeutic programme in early cases. It is noticeable that some institutions have discontinued the use of insulin altogether. In the United States of America 34 per cent of the hospitals reviewed by L. Kolb and V. H. Vogel (1942) report its abandonment. In Great Britain its abandonment has not been always due to the exigencies of the war.

Risks.—It is probable that both the advantages and the dangers of shock therapy have been exaggerated. The death rate with insulin has been six per thousand, and with electrical convulsion therapy 0.5 per thousand. The chances of serious fractures in convulsive shocks are very small when proper precautions are taken. Some hospitals are now using a jacket with sleeves but the immobility so produced may favour fractures. Physical illness, sepsis, prophylactic inoculations given forty-eight hours previously and suspicion of tuberculosis are all contra-indications (R. E. Hemphill, 1942). Even bony disease of the spine is not necessarily a contra-indication. A. Meyerson (1942), for example, has treated a man of seventy with osteitis deformans. The use of curare to paralyse the nerve termination in muscles, or the use of a spinal anaesthetic, suggests itself as limiting the risk of fracture in such cases. W. Goldfarb and K. M. Bowman (1942) object to the use of curare in electrical convulsion therapy, stating that the electrical method depresses the respiratory centre in a way that leptazol does not. In surveying the results of 1,600 cases in which patients were given shock

therapy of various kinds in the mental hospitals of Ontario, where there are 16,000 patients in residence at one time, L. Penrose found that in consequence of the shock treatment employed during the period 1938-41 there were at least 100 patients fewer in residence in 1941-2 than there otherwise would have been. He concludes that very little basis yet exists for the view that shock treatment has value in schizophrenia.

Technique

The use of intravenous insulin, with intravenous glucose for the interruption of coma, followed by feeding with potato soup is advocated by R. A. Sandison and J. S. McGregor (1942), on the ground that it saves insulin, obviates the danger of delayed recovery and late shock, and allows the carbohydrate intake to be lowered. There is less restlessness, and the long period of confusion subsequent to recovery from intramuscular insulin with nasal feeding is avoided. Sandison and McGregor regard the mechanism as one of stimulation of autonomic function. By a study of the gastric juice during treatment, they claim to have shown that insulin given intravenously is a more powerful autonomic stimulant than insulin given by the intramuscular method.

Electroencephalogram in electric shock therapy

Patients subjected to a generalized convulsive seizure exhibit changes in their electroencephalograms similar to those observed in spontaneous convulsions, and an electroencephalogram previously normal returns to an approximately normal state in from fifteen to thirty minutes. The larger the series of treatments the more noticeable become the abnormalities, and the greater the time for which these persist. The type of wave that develops consists of a slow 2 to 4 per second cycle of moderately high voltage. In epileptics the spontaneous *grand mal* and *petit mal* seizures increased in a few days after an electrical convulsion had been given, and one patient showing a suspicious electroencephalographic pattern beforehand developed a spontaneous generalized convulsion four weeks after the last electric shock treatment had been given (B. L. Pacella and S. E. Barrera, 1942).

Amytal as a prognostic test

The use of amytal to determine the likelihood of a favourable response to shock methods has been tried again. The appearance of a positive reaction consisting in euphoria and a greater accessibility is considered to be a good omen in schizophrenics whom it is proposed to submit to electric shock treatment. The dosage used is 0.65 gramme in 10 cubic centimetres of distilled water injected at a rate not exceeding 1 cubic centimetre per minute up to a maximum of about 3.8 cubic centimetres.

Effect of electric shock on the brain

It is clear from clinical observation of the disturbance of memory which occurs after electrical shock treatment that some amount of brain damage is produced. That this may involve structural alteration is suggested by the examination of the brains of dogs to which electric shock is given, comparable in strength and frequency to the shocks given to patients. The changes produced in nerve cells consisted of pallor, swelling, vacuolation and tigrolysis with some areas of actual destruction. Occasionally there was damage to myelin and in other cases there were haemorrhages in the cortex, the meninges and round the ventricles. The changes nevertheless appeared to be reversible for the most part. It is doubtful whether these observations really apply to clinical work since the animals received a dosage of current of the same order as that given to man.

GROUP PSYCHOTHERAPY

The exigencies of war, with shortages of staff, have brought into prominence the problem of giving psychotherapy to groups rather than to individuals. One experiment consisted in taking a group of fifty patients on three occasions per week. A talk by the doctor was followed by general discussion. The talk consisted of an elementary description of the physiology of emotion. By using concrete illustrations in this way it was claimed that the patients were able to see that they had some responsibility for the way in which they regarded their visceral discomforts: they were patients in the Forces, usually with cardiac syndromes. By these means their hypersensitiveness was diminished, and a greater proportion returned to duty than had been found possible when individual psychotherapy was employed. The help of the nursing staff was enlisted for the discussion (M. Jones, 1942).

This rather physiological type of approach is not the only one that has been used. In some centres psychoanalytic concepts have been employed, P. Schilder (1939)

having done this for some years at the Bellevue Hospital, New York. In others a comprehensive programme of activities including dancing, music (broadcast through the wards), physical training, group games, dramatic shows and in some places an attempt to make the hospital conditions approximate to those of normal living, with shops, beauty parlours, cafés and the like, has been found to be beneficial (R. D. Halloran, W. Corwin and E. V. Semrad, 1942). The principle has for some years been elaborated in the Hartford Retreat in Connecticut on an extensive scale, and embodied in the sub-title of the hospital, 'The Institute of Living'.

If such methods imply an optimism hardly compatible with the constitutional origin of the illness of many of the patients in mental hospitals, it implies also that the influence of external factors, which is not inconsiderable even in these, is not neglected. If some sceptics point out that such methods are mainly an elaboration of old principles it is relevant to retort with the analogy from the devices of modern war that if you look diligently enough you can find precedents for the use of most of the modern weapons; whether we win the war or not depends upon how we elaborate and organize their use.

In a commentary on the various group methods that have been used it has been remarked that the particular method, whether psychoanalytic, persuasive or otherwise, seems to be less important than the manner in which it is administered (J. R. Jacobson and Katherine W. Wright, 1942). In some hospitals each individual case is considered in the presence of the other patients; the patient is encouraged to put his own case and the others are invited to make comment. It is doubtful if this system would be a success in our more reserved culture, but N. Blackman (1942) claims that it works in the United States of America.

PREVENTION OF PSYCHONEUROSES

The prevention of neurosis has not received as much attention in the past as it should have. There is great need for planned investigation of this topic. It has always seemed to me that the child guidance activity so characteristic of recent years has had to be taken very much on trust. Just what its ultimate effect on the reduction of neurosis in after life may be can be ascertained only by a carefully planned programme covering many years, with satisfactory controls. Apart from some work by W. Healy (1940) in the United States of America and occasional prognostic studies in Great Britain little has been done. This is not the fault of the child guidance movement so much as of the general organization and stage of development of the medical services. In default of established facts it is necessary to rely on general principles—and indeed this is not more than is constantly done in general Medicine—but long-term comprehensive valuations of the effects of treatment are not so plentiful as they might be.

Influence of faulty habit formation

Programmes of mental hygiene, such as those suggested by M. Moore (1942) are apt to have a common-sense appearance; for example, 'Children should be taught to relax and concentrate when necessary'; 'Parents should guide their children all along the line'; and so forth.

The fascination of psychoanalytic concepts in recent years has obscured the possibility that faulty habit formation may be a far more frequent cause of neurosis afterwards than would be imagined from the literature and practice of modern psychotherapy. On the other hand, it is extremely doubtful how much mental hygiene can do to avoid the largely accidental miscarriages of psychological development that produce a neurosis based on Oedipus situations and the like. Moore's programme, however, puts psychotherapy in an ideal state of things in its proper place, in which it would be reserved for individuals who, in spite of a sensible upbringing (including enlightened preparation for marriage, such as for example inculcation of the qualities to be looked for in a mate, to which should be added what is expected in oneself), develop nevertheless a neurosis.

PROGNOSIS IN MENTAL ILLNESS

Increasing accuracy of prognostication is an aim of undying importance in clinical medicine. The introduction of shock therapy continues to stimulate study of the prognosis of mental disease in its more serious form.

Again there is a need for well organized research in these problems with proper statistical control. Not only syndromes but individual symptoms need to be studied

in relation to ultimate outcome. The numbers studied in this way are usually too small, or if not too small they are not given the necessary statistical elaboration. Thus, A. B. Carter (1942) studying seventy-eight adolescent psychoses came to the conclusion that no single syndrome and no one factor decides the outcome, but that the final result is at least favourably influenced by sound heredity, a sound tradition, a pyknic physique, favourable associated factors including fortunate economic conditions, and an acute onset with the preservation of appropriate emotional responses. This is in accord with general experience.

MANAGEMENT OF PSYCHOSES IN PRACTICE

Psychoses so seldom occur in the experience of the general practitioner in contrast to psychoneurotic and psychopathic conditions, that he does not have much chance to acquire skill in the diagnosis and management of them. With this in mind A. Harris (1942) has proffered some useful advice on the indications for removal to a mental observation ward.

Features of a psychosis

It is particularly important to know how to recognize a psychosis, that is a primary mental disease as distinct from the effects on brain function of some physical illness, such as acute fever producing delirium, or a chronic brain disease mainly responsible for failure of memory but sometimes also signalized in its early stages by small departures from normal behaviour. Mild infections may produce delirium in susceptible people; alcoholics are among the most susceptible, and apart from the classical delirium tremens the alcoholic probably has a threshold for the development of delirium lower than that of the average person with an acute infection.

While most acute fevers produce physical signs of their own it must be remembered that meningitis may produce delirium without fever or neurological signs. The history of headache, vomiting and pains in the limbs is important and is quite different from the premonitory stage of a psychosis, such as schizophrenia or a manic-depressive condition. Some 'hysterical' or over-emotional individuals may respond to acute pain in a way suggesting mental rather than physical disease. Congestive heart failure can produce confusion and delirium, which subsides under appropriate physical treatment, and it is embarrassing if such patients have been unnecessarily removed to a mental observation ward. Nevertheless, in some cases of delirium from physical disease the excitement and restlessness may be so extreme as to make nursing under ordinary auspices impossible. It should be added that the provision of psychiatric wards or units in general hospitals would do much to meet this difficulty. Sometimes foreigners with an imperfect knowledge of English are mistakenly regarded as having mental disease and sent to observation wards.

The general practitioner should remember that occurrence of delirium does not provide sufficient grounds for compulsory treatment unless it causes interference with the community.

Problem of the suicide

One of the problems which most commonly recurs is the safeguarding of depressed patients from suicide. This is all the more difficult as such patients are often completely lucid, and may not have any delusions. A suicidal risk, however, which occurs in a state of obvious and persistent depression of spirits is an adequate reason for placing a patient under observation on a three-day order to begin with. The trouble is that the law as it stands allows the public assistance officer to have the last word in the matter, and to override the judgment of the doctor—a very curious state of affairs, which sometimes has had disastrous results.

Knowledge of drugs

Better acquaintance on the general practitioner's part with the uses of drugs would be a great help in cases both of delirium and of psychotic excitement (Harris). In the case of a delirium resulting from physical disease the giving of morphine and hyoscine combined, or paraldehyde, 2 fluid drachms or more by mouth, or 4 fluid drachms or more of freshly prepared paraldehyde in a suitable vehicle per rectum, may tide over the difficult period in delirium and toxic mental states. Barbiturates are not suitable for delirium secondary to toxic or structural brain disease, whereas in psychoses they are often effective if properly used, and in the event of the patient refusing to take them by mouth they can be given either intramuscularly or intravenously; but

the latter route requires special experience, as here the procedure is equivalent to the giving of a mild anaesthetic.

PSYCHOPATHOLOGY

In a review of 100 women who had acquired before the age of thirteen some general physical handicap, such as spastic paralysis, heart disease or epilepsy, it has been shown that there is not any specific effect from any particular type of handicap, but a general tendency to immaturity, including psychosexual immaturity. There was no evidence that the delay in sexual development had a special influence on the general psychological make-up—rather a surprising conclusion and a counterblast to certain popular misconceptions that immature psychosexual development is usually accompanied by neurotic symptoms. The role of constitution and of habit formation in personality development is emphasized as a result of this systematic study, and the essential individuality of the product of personality development is also demonstrated (C. Landis and M. M. Bolles, 1942).

HOMOSEXUALITY

A well coordinated study of this hitherto not systematically explored territory has been made by G. W. Henry (1941).

The general factors producing homosexuality are (1) constitutional deficiencies—structural, physiological and psychological; (2) the influence of family patterns of sexual adjustment (for example a large proportion of masculinity in the females and of femininity in the males of a family is most likely to result in sex variants among the succeeding generations); and (3) lack of opportunities for psychosexual development. There is no adequate substitute for well-adjusted parents, whose responsibility it is to see that the sex education of the child is begun early and continued until a good adjustment obtains. This is a matter to which, strangely enough, insufficient attention has been paid in psychopathology generally. Again, preoccupation with inner factors, and to some extent with hereditary ones, has blinded investigators to the influence of precept, of example and of the subtle effects of disorganization of the normal emotional patterns within the family. It is psychologically inaccurate to specify persons as wholly male or wholly female, the relative proportion of masculine and feminine traits has to be gauged. Cultural factors play a part in the production of homosexuality, such as religious and moral taboos on heterosexual knowledge.

The M-F test of Terman and Miles indicates that the variant is intermediate between male and female in its psychological qualities. Physically there are evidences of a constitutional basis, for example some internal diameters of the pelvis in women are smaller in female homosexuals than in obstetrical patients.

CONSTITUTION

This is a particularly difficult matter to study because of the large number of variables and consequently of the enormous number of combinations of characteristics, physical and psychological, that are possible. On the physical side there is one sign that is reassuring in its constancy in a sense, namely that each new investigator seems to repeat old observations, mainly with slight differences in terminology, so that the old concepts are given a broader foundation. The now well known division by E. Kretschmer (1925) of individuals into pyknic, athletic and asthenic types is only a re-echo from another quarter of the work of older students of constitution. The latest attempt in this direction (W. H. Sheldon and S. S. Stevens, 1942) seems to disentangle the same general types, but this time calls them viscerotonics, somatotonics and cerebrotonics, and with the additional statistically evolved finding that there is a correlation as high as .80 between these physical types and three types of 'cluster' of temperamental characteristics, which they distinguish by a process of factor analysis.

Classification

The three groups with their accompanying mental qualities are described as follows.

Viscerotonia.—Characterized by general relaxation, love of comfort, sociability, conviviality, gluttony for food, for people and for affection—the personality here seems to centre around the viscera.

Somatotonia.—Characterized by a predominance of muscular activity and of vigorous bodily assertiveness—the personality seems dominated by the soma.

Cerebrotonia.—Characterized by a predominance of the element of restraint, inhibition and desire for concealment; these individuals repress somatic and visceral

expression and their behaviour seems dominated by the inhibitory and attentional functions of the cerebrum.

INTELLIGENCE TESTS IN PSYCHOSES

There has been a fashion recently in the application of intelligence tests to psychoses, not simply of the organic but of the 'functional' or 'biogenic' types (manic-depressive and schizophrenic mainly). The application of intelligence tests to patients with an organic psychosis, that is, one dependent upon structural brain alteration, has had some success, since such psychoses are commonly associated with intellectual failure; but the sense of the procedure in functional psychoses is a little dubious since these tests depend not only on intellectual capacity but on volition, that is whether the patient can or will attend to the tests in spite of his preoccupations or his reluctance. In recording therefore that the mental test pattern is remarkably constant in developed psychoses with vocabulary highest, verbal ability testability second, and non-verbal test ability lowest, it is well to remember that test behaviour is strongly correlated with cooperation, and that these findings may not represent a true deterioration. It has also to be remembered that difficulties in these tests with psychotics may depend, not upon intellectual disablement but upon diminution in the available 'G' or 'energy' behind intelligence. M. B. Brody (1942) points out that the alleged 'scatter' of test performance in psychotics is not proven.

Intelligence tests have been used in helping in the prognosis of shock therapy; when patients preserve their capacity for conceptual thinking the prognosis is considerably better.

In a similar study with the Stanford-Binet test in 827 psychotics A. Roe and D. Shakow (1942) found that the more severe and psychotic condition the worse the psychometric performance.

Deviation from the normal is less in vocabulary tests than it is in others, but that it is not an adequate reflection of the previous level is shown by the fact that in hebephrenics and general paresics it is far below the level of previous education. Repetition of digits forwards is especially affected in psychoses.

In general, however, the types of performance most affected are conceptual thinking and immediate memory. Those least affected were items learned of old, for example vocabulary. But the only type of psychosis in which Roe and Shakow found a large general falling off was hebephrenia, whereas in other types of schizophrenia there was little departure from the normal. It seems therefore that the application of such tests to functional psychoses is of dubious practical advantage.

PSYCHIATRY IN WAR

Effect of air-raids

The war has produced voluntary and involuntary psychiatric experiments on a large scale. The general evidence is to the effect that there has been very little increase in the incidence of neurosis or mental disease generally as the result of exposure to air-raids (R. D. Gillespie, 1942; A. Lewis, 1942). On the whole any increase which has occurred has been produced less by danger than by the anxieties associated with the break-up of homes, and so forth, including especially the separation of children from their parents and by the disorganization of the settled lives of unstable or elderly persons. It has been noted that the incidence of neurotic illness has been low in Civil Defence workers (Lewis). There is no evidence of any general increase in alcoholism. The most notable rise in any field is in that of juvenile delinquency, as the result of the absence of parents and the removal of many of the recreational and educational facilities of peace time. Predisposition counts for a good deal, in both civilians and soldiers; thus in three-quarters of the neurotic patients presenting themselves to a general practitioner during the London 'blitz' three-quarters had had previous neurotic illness: most of the previously sound individuals improved or recovered, while only a quarter of the pre-disposed did so (Whitby). There is some evidence that suicide has diminished.

Group intelligence tests in the Forces

So far as the Forces are concerned, psychological conditions bulk very largely in invaliding, forming a third of the total discharges on medical grounds, for example from the Army (J. R. Rees, 1943). The necessity for weeding out defectives especially has brought selection processes into play, so that group intelligence tests are now given as a routine at some stage of recruitment. These group intelligence tests are a very satisfactory means of detecting the dull and the defective, who can then be given

an individual examination to decide whether they can be used at all, and if so, in what way. The Army has formed special unarmed labour sections for dull individuals, and in these they even adjust happily. For skilled trades aptitude tests are given, and the whole procedure, with psychometric tests correlated with job analysis, has been carefully systematized in the Army, while similar arrangements exist in other Services. The Army Medical Service now includes a Directorate of Army Psychiatry.

Psychosis in the Forces

It has been noticed in the present war, as it was in that of 1914-18, that the prognosis of psychoses occurring acutely after admission into the Forces is commonly favourable. The fact that a considerable proportion of those who develop psychoses have had similar illnesses in civil life points to the need for a more comprehensive method of screening such people from military service altogether; this could be done satisfactorily however only if health records were available to recruiting boards, and in an ideal state of affairs records of any prison sentences should be available as well.

A 'follow-up' study has been made of neurotic soldiers returned to the Army after treatment, in comparison with a group who had to be discharged after receiving treatment. It was concluded that the following attributes were of bad prognostic omen: positive family history; unsatisfactory work record; psychopathic traits of personality; symptoms of the present illness before enlistment; previous dislike of army service; keenness to get back to army duty; exposure to Dunkirk conditions or other severe stress of bombardment and active service; querulous hypochondriacal complaints; fugue or amnesia; surly or paranoid attitude. The fewer of these attributes the patient has, the greater likelihood of his remaining in the Army. The evidence, however, does not indicate that prognosis can be based safely on the number of these attributes a patient is found to possess. The intensity with which each attribute has been exhibited, its nature, and the favourable attributes also discovered must be considered. The findings do not have regard to the varying conditions of army life to which the soldier returns, and these are also of prognostic importance (A. Lewis and E. Slater, 1942).

MENTAL SYMPTOMS AS A RESULT OF BLAST

In a survey of psychiatric syndromes becoming evident after blast without head injuries F. W. Anderson (1942) has described symptoms pointing to cerebral damage: (1) residual intellectual impairment, (2) memory changes; (3) less certain evidence of slight and transient aphasia in two cases; (4) occasional changes in the cerebrospinal fluid. One patient, some weeks after the incident, had a dissociative sleep-walking experience, and an increased liability to alteration of consciousness while under the influence of alcohol. In addition apathy and general slowing down were noted. Treatment consists of at least two weeks' complete rest in bed with sedative treatment along psychiatric lines (Anderson).

MALINGERING

Malinger, which is uncommon, has been discussed by R. Good (1942) who thought that his patients showed a morbid desire for punishment and retained infantile dependence, particularly on the mother. In other words they were emotionally immature people; it seemed unlikely that either treatment or punishment would have any deterrent effect on repetition of the malinger. For this reason, and also because of the effect on his fellow-soldiers, Good thinks that a malingerer should be removed from the unit. The consequences to the others of the knowledge of his discharge from the Forces have, however, very seriously to be considered.

ELECTROENCEPHALOGRAPHIC STUDIES OF PSYCHOPATHIC INDIVIDUALS

The evidence continues to accumulate that the electroencephalogram is abnormal in a considerable proportion of psychopathic individuals, both children and adults, more especially in the aggressive types (R. L. Jenkins and B. L. Pacella, 1943).

PSYCHOSOMATIC MEDICINE

The interest in the share of psychological factors in the precipitation and perpetuation of actual physical disease continues, and conditions such as those mentioned below have been shown often to have important psychological components in their aetiology. The most common finding, apart from severe and psychological trauma as a precipitating factor is that individuals suffering from these conditions are fairly often of obsessional personality, often with a great deal of energy and a pathological con-

science which makes them use their energy to the utmost. Their propensity to develop anxious tension is another factor. In 300 consecutive cases admitted to a general hospital 78 per cent had some psychological factor in their aetiology (L. A. Schwartz, 1942). In 1,003 cases of dyspepsia in the Royal Navy H. J. Wade (1942) emphasized the greater incidence of psychological factors in duodenal as compared with gastric ulcer. Nervous dyspepsia without physical lesion also is not a gastric disease but simply a state of anxiety reflected on the gastric function (Wade; J. E. Finesinger, 1942).

The explanation given for the development of ulcer by S. Morrison and M. Feldman (1942) is as follows: repeated duodenal irritability leads to ischaemia and loss of local viability, which when acted on by irritating boluses and acid, finally culminates in necrosis of tissue and consequent ulcer. The play of impulses from the autonomic and central nervous systems upon the duodenum is often the initiator of the process.

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THE AUTONOMIC NERVOUS SYSTEM

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PERIPHERAL VASCULAR DISTURBANCES

Peripheral circulation

In an account of the peripheral circulation, including the lymphatics, S. Freeman and F. S. Grodins (1941) state that the arterioles in all digits of all extremities undergo simultaneous periodic constrictions, accompanied by cardiac acceleration and a rise in blood pressure. This phenomenon is mediated entirely by the sympathetic nerves, and is independent of skin temperature and of external and psychical stimuli. The 'volume pulse' of a part is defined as the difference between the arterial inflow and venous outflow in that part, in one cardiac cycle. When the environmental temperature rises, the amplitude of the volume pulse rises and the frequency of these periodic constrictions becomes less. Thus the elimination of heat leads to a modification of the rhythmic fluctuations described. In a discussion of the findings of other writers, the authors draw attention to the following points. A protein meal (D. I. Abramson and S. M. Fierst, 1941) led to an increased blood flow in the forearm and leg when the experiment lasted more than one and a half to two hours, whereas a carbohydrate meal did not have this effect.

Reflex vasodilatation.—Reflex vasodilatation (D. I. Abramson, H. Zazeela and J. Marrus, 1939) caused by heating some other part of the body, is maximal in the hand, less in the foot and least in the forearm; this confirms the findings of others. It has been stated (G. W. Wright and K. Phelps, 1940) that nerve block produces better vasodilatation than does the reflex method. When a limb is heated to 45° C., the resultant blood flow is greater in the hand than in the forearm, and greater in the foot than in the leg (Abramson, Zazeela and Marrus; P. Kunkel and E. A. Stead, Jun., 1938; P. Kunkel, E. A. Stead, Jun. and S. Weiss, 1939); since the hand and foot contain relatively more skin, and the forearm and the leg relatively more muscle, it is thus concluded that the resultant flow is greater in skin than in muscle. At 32° C. some workers (Kunkel, Stead and Weiss) found a greater percentage increase in the hand than in the forearm; others (Abramson, Zazeela and Marrus) found the opposite. Changes in the volume of the limbs may be due to alterations in the venous calibre (D. I. Abramson and K. H. Katzenstein, 1941), not necessarily to alterations in the blood inflow.

Vasoconstriction.—Deep breathing, puffing at an unlit cigarette (F. E. Franke and A. B. Hertzman, 1940), and inhaling denicotinized cigarettes (M. G. Mulinos and I. Shulman, 1940) produce peripheral vasoconstriction as great as, or greater than, that caused by actual smoking; this is most apparent in the fingers (Franke and Hertzman), less so in the hands and feet (D. I. Abramson, H. Zazeela and B. S. Oppenheimer, 1939), slight in the forehead (Franke and Hertzman), and not perceptible in the forearm (Abramson, Zazeela and Oppenheimer). When the method of photoelectric plethysmography was used (A. B. Hertzman and J. B. Dillon, 1940) in the study of arteriosclerosis and Buerger's disease, it was found that the 'maximal' blood flow to the foot could be reduced to 50 per cent without the occurrence of symptoms or of nutritional changes (Kunkel and Stead, Jun.); when the flow was reduced to 33 per cent symptoms and nutritional changes usually appeared.

Sympathetic denervation of arm

Preganglionic denervation.—The problem of producing complete and lasting sympathetic denervation of the upper extremity by preganglionic section is discussed by R. H. Smithwick (1940). His most recent modification of preganglionic denervation is intraspinal root section, the immediate results of which are satisfactory and complete: after two or three years, however, examination showed that in some cases moderate to marked regeneration had occurred. The author divides the second and third intercostal nerves, and dissects them towards the intervertebral foramina, cutting their rami communicantes as they are encountered. He then sections their posterior roots proximal to the posterior root ganglia, and teases out the intraspinal parts of

their anterior roots. The sympathetic trunk is divided caudal to the third thoracic ganglion, and the second and third thoracic sympathetic ganglia (now decentralized) are covered with a fine silk cylinder to guard against regeneration. Even with regeneration, which is rarely complete, the blood supply to the limb is improved.

Sympathetic innervation of upper extremities

C. Van Buskirk (1941) gives an account of the nerves in the vertebral canal and their relation to the sympathetic innervation of the upper extremities. The author used cats as his experimental animals. He found that most of the fibres of the recurrent branches of the rami communicantes end in relation to blood vessels and supporting connective tissues within the vertebral canal; some penetrate the vertebrae and some join the anterior roots of the spinal nerves at levels higher than that of the foramen through which they entered the vertebral canal. These last fibres are unmyelinated; in the thoracic region they may ascend through as many as six or more segments before joining an anterior nerve root. This finding tends to confirm J. C. White's statement that complete sympathetic denervation of the upper limb in monkeys, by section of anterior nerve roots of thoracic nerves, requires section of all roots as far down as the twelfth thoracic segment. H. D. Kirgis (1941) reports, from many dissections on human beings, that the third thoracic nerve gives a slender ramus which joins the second thoracic nerve near the junction of the second and its ramus communicans; it contains many unmyelinated fibres, and provides one pathway through which fibres arising in the third or lower thoracic ganglia may reach the upper limb. If this ramus is removed, the only sympathetic fibres which can reach the upper limb must arise at lower levels, ascend in the vertebral canal and join the nerves of the upper extremity through intervertebral foramina in the thoracic and lower cervical segments.

Raynaud's syndrome

Clinical picture and treatment.—C. A. Johnson (1941) presents a study of the clinical manifestations and of the results of treatment of twenty-two patients with symptoms of Raynaud's syndrome. The author does not draw any conclusions from so small a series of cases, but considers that certain of his findings are of no significance, in the light of other published cases. He states that in Raynaud's syndrome the disturbances are found in the hands or in the hands and feet, but never in the feet alone. The majority of cases occur in patients between the ages of twenty and fifty years, the commonest decade being from thirty to forty. There was a positive family history in three instances. The author considers that treatment should be directed towards (1) relief of mental anxiety, which was effective in three out of the twenty-two patients; (2) treatment of anaemia (thirteen of the twenty-two patients had mild secondary anaemia and effective treatment of this condition produced relief of symptoms); and (3) treatment of associated specific disease, especially syphilis. Five patients out of the series of twenty-two cases were treated by sympathetic denervation, but in the light of most recent work not one of the five different types of operation was an anatomically complete sympathetic denervation, a fact which the author apparently does not realize. The vessels regained their pre-operative tone and the circulation returned to its pre-operative level in from seven to twenty-one days, although the skin temperatures remained higher and the skin temperatures on subsequent median nerve block were variable; sweating after operation was also variable. The author concludes, from unsatisfactory evidence, that operative treatment is of little value. He also considers that the symptoms in Raynaud's syndrome are those of some more fundamental disease; they may be due to the palmar arches becoming dilated and acting as a blood shunt, the result being that the digital vessels collapse because of insufficient blood supply and blood pressure. He quotes a number of facts in evidence and considers that the somatic nerves may have a vasomotor function, since post-operative median nerve block may (two cases out of twenty-two) produce vasodilatation.

Peripheral arterial occlusion

Peripheral arterial occlusion is discussed by G. P. Pennoyer (1941). He states that metabolite control of the circulation, when tissue nutrition is impaired, puts in abeyance the sympathetic control, and that vasospasm does not play any part. Hence the treatment of demarcated gangrene should be by a thermostatically controlled bed cage, kept at 92° F., which, he says, prevents rise of local metabolism and vasospasm; the patient should rest in order to reduce the nutritional needs of the tissues; Buerger's exercises are not indicated, but the oscillating bed is valuable.

Traumatic arterial spasm

S. M. Cohen (1940-1) discusses traumatic arterial spasm. He considers that violent methods of traction, for example in compound fractures, may precipitate arterial spasm which may endanger the life of the limb and may be conducive to the development of gas gangrene. In arterial obliteration, arteriectomy after twenty-four hours is probably doomed to failure (four recorded cases since 1935). This valuable paper should be read in full by those interested in the subject.

Acute embolic occlusion of arteries of extremities

L. N. Atlas (1942) describes the management of acute embolic occlusion of the arteries of the extremities and advocates, as treatment in the acute stage, the giving of papaverine hydrochloride, $\frac{1}{4}$ grain (0.016 gramme), four-hourly for forty-eight hours, and thereafter three times daily for a week. Heparin is given to prevent thrombosis in the collateral vessels by keeping the coagulation time at not less than fifteen minutes. Heat is not applied. Treatment after the acute stage has passed off, when colour is returning, consists in the application of mild local heat, rhythmic venous occlusion and the provision of a suction pressure boot. Finally, the author states that failure of the above treatment means that an organic block rather than spasm is responsible, in which case he advises operation.

Treatment of phlebitis by novocain

E. C. Dalsgaard (1941) gives an account of treatment of phlebitis of the lower extremities by paravertebral injection of the lumbar sympathetic ganglia with novocain (procaine hydrochloride). For this line of treatment the author claims the following results in twenty of his own cases: the immediate cessation of pain; the rapid cure of the phlebitis; less frequent and less severe complications; diminished danger of embolism, no lung infarcts and finally no harm.

THE HYPOGASTRIC PLEXUS**Anatomy of superior hypogastric plexus**

B. B. Weinstein (1942) describes the surgical anatomy of the superior hypogastric plexus, and reports 150 personal dissections.

General anatomy.—All the lumbar sympathetic ganglia give contributions to the superior hypogastric plexus, but the preponderance is from the upper two ganglia. In the author's series the sympathetic trunk itself gave branches to the superior hypogastric plexus in only three; of these two were bilateral and one was unilateral (left). The branches were short and fine, and ran directly from the trunk to the plexus. Fibres from the lumbar sympathetic ganglia pass downwards and medially, posterior to the corresponding common iliac artery but anterior to the vein. Exceptions occurred in eight cases; in five the fibres were posterior to both the artery and the vein, and in three they were anterior. Only six received branches from the sacral sympathetic chain; all were from first sacral ganglia. The superior hypogastric plexus divides below into the right and left inferior hypogastric nerves, which furnish the sympathetic nerve supply to the ureters. On each side the inferior hypogastric nerves pass to the medial aspect of the plexus of Frankenhäuser as it lies on the side of the rectal ampulla. From its medial side this plexus provides the pelvic visceral sympathetic supply; on its lateral side it forms an extensive anastomosis with the sacral nerves. The superior hypogastric plexus sends filaments to the periarterial plexuses as follows: the superior rectal into the sigmoid mesocolon; the middle sacral, infrequently; the external iliac (in seven cases); and all branches of the hypogastric. Afferents from all the pelvic viscera traverse the superior hypogastric plexus, except ovarian afferent fibres, and possibly lateral fibres from the uterine (Fallopian) tubes. The ovarian fibres run in the periarterial ovarian plexus in the suspensory ligament of the ovary; they are joined by a lateral tubular branch, and reach the spinal cord at the tenth thoracic segment. The uterine afferent fibres traverse Frankenhäuser's plexus and the superior hypogastric plexus to reach the spinal cord at the tenth thoracic to the first lumbar segments.

Plexus morphology.—The plexus is situated in the interiliac triangle, the apex being formed by the junction of the mesenteric nerves and the base lying where the main fibre groups diverge to end in the inferior hypogastric nerves; that is at the sacral promontory. It is always prelumbar, not presacral. In most of the cases (88 per cent) it was an actual plexus; in 8 per cent it consisted of bilateral cords; and in 4 per cent there was a single presacral nerve. It was single (from apex to base) in 2 per cent, but even then consisted of unconnected nerve bundles (L. Elaut, 1932). In 3 per cent two

nerves entered the apex, joined to form one after from 1 to 1.5 centimetres, and bifurcated at the base. In 8 per cent there was a double cord separated throughout; these cords had very fine anastomoses throughout the whole triangle. In 4 per cent the lateral components were well marked and there were many thick connecting fibres. The intermesenteric nerves fuse at the apex; almost immediately they bifurcate and diverge, but are connected by many fibres, thus forming a triangle. This triangle was narrow in 29 per cent of cases, wider in 35 per cent, and in 2 per cent there was a spider-web formation with marked divergence and with very fine connecting fibres. The plexus was arch-shaped in 1 per cent. In 8 per cent the entire plexus was shifted to the left of the midline and was immediately adjacent to the left common iliac artery; such a position introduces a danger of inadequate removal. In 8 per cent the intermesenteric nerves continued downwards into the triangle, as multiple parallel bands. These were connected by many fibres and fused just above the promontory.

Surgical anatomy.—The nerve plexus lies in fibro-fatty tissue. The left common iliac vein lies behind this, and between the two is a line of cleavage. The middle sacral artery is more palpable than visible, whereas the nerve fibres are more visible than palpable. The right ureter crosses the right common iliac artery just above its bifurcation; it is adherent to the peritoneum and comes forward with it, unlike the nerve fibres. There are three types of mesocolon: (1) short, easily retracted to the left to give adequate exposure (found in from 75–82 per cent of the present series); (2) long, readily shifted and retracted to give adequate exposure (14.25 per cent); and (3) long, leaving the embrace of the interiliac triangle and attached along the midline (1–15 per cent). The last type is dealt with by an incision parallel to the root of the mesocolon and through both of its layers to avoid danger to the nervous and vascular supply of the pelvic colon. The author found certain anomalies in his series. In four cases there were accessory ureters running across the triangle. A transverse duodenum anterior to the triangle was found in three cases, in one of which the other viscera were also ptosed. In 14 per cent of cases the left common iliac vein projected well into the triangle beyond the midline and adopted an 'S' shape. The left common iliac artery followed a similar course in 2 per cent of cases, and was then covered anteriorly by the superior hypogastric plexus. In one case the right and left common iliac veins joined to form the inferior vena cava anterior to the aortic bifurcation. Anomalous veins were present in twenty-six out of the 150 cases, and varied in size from small to half that of the common iliac vein. Their origin and course varied as follows: origin within the right psoas muscle, crossing the pelvis and entering the right common iliac vein; origin from the periosteum, running across the interiliac triangle and entering the common iliac vein; and accessory haemorrhoidal veins lying retroperitoneally to the left of the midline in the triangle and entering the left common iliac vein.

Trigonal muscle

D. Macleod (1941) discusses the trigonal muscle, with special reference to its composition and urinary function, and states that this muscle consists of two physiological units with a single anatomical derivation from the longitudinal muscle of the ureter. Its motor innervation is derived from the presacral nerve, and sensory innervation from the presacral nerve and the parasympathetic nerves (second and third sacral). Although the motor supply of the trigone is purely sympathetic, yet it contracts during detrusor action which is entirely parasympathetic. Since trigonal action opens the internal meatus, it must be controlled by the local vesical plexus.

ANAESTHESIA

Splanchnic anaesthesia

R. Engel, D. B. Phemister and H. Livingstone (1941) give an account of splanchnic anaesthesia. They state that splanchnic anaesthesia affords analgesia of the stomach and intestines, the kidneys and the adrenal glands; it also affects the cardiovascular and metabolic functions of the entire organism because of the mixed character of the splanchnic nerve fibres. The use of Braun's anterior approach is advocated, and splanchnic anaesthesia is advised for gastric, splenic, pancreatic and biliary operations in the aged and in those suffering from pulmonary disease, cardiovascular disease, anaemia or severe cachexia. Its use is contra-indicated in abdominal exploration, lower abdominal operations, peritonitis, intestinal obstruction and in very obese patients. The authors quote fifty-seven cases: in thirty-five there was adequate anaesthesia, in eight there was partial anaesthesia, and eight were failures. The advantages claimed

are: little reaction at operation, smooth post-operative course, few complications and absence of danger if intravenous injection is avoided. Finsterer's method is described as follows: infiltrate the abdominal wall with novocain; make a small incision; insert the left hand and place the index finger on the body of the twelfth thoracic vertebra, separating the aorta and the inferior vena cava; pass the needle along the radial edge of the index finger until it reaches the vertebra, and inject after making certain that the point of the needle is not in a vein; 50 cubic centimetres or more of from $\frac{1}{4}$ to $\frac{1}{2}$ per cent novocain with adrenaline is injected.

Splanchnic anaesthesia and abdominal pain

An account of abdominal pain and of thoracic splanchnic anaesthesia is given by O. Hultén (1942). The author believes that, in intra-abdominal lesions, the relief afforded and the analgesia produced by a local anaesthetic in the abdominal wall is due to the abolition of muscular spasm, and that 'mesenteric' pain is mediated by the perivascular mesenteric plexuses. Probably only the splanchnic nerves transmit pain from the abdomen, and not the vagi or phrenic nerves. To anaesthetize the abdominal cavity, interruption of both splanchnic and spinal nerves is necessary; this can be accomplished most easily by a spinal anaesthetic regulated to reach the level of the fifth thoracic segment. The disadvantage is lowering of blood pressure, and the author claims that this does not occur when splanchnic anaesthesia is combined with infiltration of the abdominal wall; he admits, however, that this does not afford such good relaxation; he prefers to use Kappis's method in cases in which spinal and general anaesthesia are contra-indicated. The anaesthetic used is 250–300 cubic centimetres of 0.5 per cent procaine hydrochloride with from 12 to 15 drops of 1 in 1,000 adrenaline. The needles should be from 12 to 15 centimetres in length. A wheal is made 7 centimetres from the spine, immediately distal to the twelfth rib. The needle is inserted at an angle of 30° towards the median plane, and possibly slightly cephalad. Five cubic centimetres is injected when the needle impinges on the lateral aspect of the vertebral body. This procedure is repeated on the other side, then the needles are advanced until they leave the vertebral body. Sixty cubic centimetres is now injected on the right side and 40 cubic centimetres on the left. The fluid spreads along the root of the mesentery and along its large vessels, and from the eighth thoracic vertebra to the third lumbar vertebra. Half an hour elapses before maximum anaesthesia is produced, during which time the anterior abdominal wall is infiltrated with the same solution, particular attention being paid to the peritoneum. The author states that the mortality rate is 1 in 10,000. He stresses the fact that it is necessary to operate with great gentleness, avoiding sudden movements, and that uniform success is obtained only after much practice and experience.

Anaesthetic procedures around the vertebral column

T. H. Seldon (1941) states that cervico-thoracic and lumbar types of sympathetic block are of both diagnostic and therapeutic value. Vasoconstrictor mixtures should not be used. He advocates induction of anaesthesia by intravenous pentothal sodium during the injections, because this allays the pain of alcohol and also prevents the dilution which attends the use of a local anaesthetic.

HEART

Cardiac symptomatology and histo-pathology in patients with mega-oesophagus and megacolon is discussed by J. Ramos and J. Oria (1941), who maintain that 'mega' syndromes are general diseases of the vegetative nervous system. They state that patients with mega-oesophagus and megacolon have abnormal electrocardiograms which indicate that the heart is actually affected, not merely deviated or compressed. In the majority there is no clinical cardiac insufficiency. Histologically they found chronic lesions in the intracardiac autonomic plexus similar to those in the intramural plexuses of the oesophagus, stomach, colon and rectum. These lesions consisted of destruction of the subepicardial and endocardial atrial and ventricular plexuses, with fibrosis of groups of ganglia, and later the development of interstitial myocarditis.

INTRA-ABDOMINAL LESIONS

Gastro-duodenal and hepato-lienal circulatory disorders occurring after lesions of the abdominal sympathetic nerves are described by G. Nicolosi (1941). In his experiments, the author used ten dogs and ten guinea-pigs. In these, the adventitia of portal

and gastro-lienal vessels was injected with lead acetate or with phenol, which causes sympathetic interruption by necrosis. This procedure led to serious circulatory disturbances of the stomach, upper small intestine, liver and spleen, with accompanying haematemesis, melaena, ulcer formation in the gastric and duodenal mucosa, and necrotic foci in the liver and spleen. The results may have been due to hormonal action resulting from nerve destruction (although this is unlikely), or to circulatory trouble. The effects simulated verified pathological conditions in human beings.

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NEUROLOGY

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The influence of the present war on the amount of new neurological work reported has been much more apparent in the past year than in preceding war years and although it is easy to understand why this should be so one cannot help being struck by the diminution in the amount of new knowledge and in the number of new ideas published since the previous Critical Survey was written. There is nothing in the period now under review to compare in importance with, for instance, the findings of de Barenne and McCulloch on the functional relationship of cortex and thalamus, or the work of Denny-Brown and Russell on concussion, which were referred to in Medical Progress (Critical Survey section) 1941-2, pp. 89 and 92. The present war has so far inspired or instigated remarkably little new work in the neurological field or at any rate such work has not been published. Investigations on peripheral nerve injuries are, however, still proceeding at Oxford, and the year's publications from this centre are mentioned below. As in previous Surveys, only those publications are referred to which contain new knowledge or give a promise of further developments.

ANATOMY AND PHYSIOLOGY

The brain of the infant

J. Le R. Conel (1941) has published a second volume dealing with the developing human cerebral cortex. The first volume dealt with the brain of the new-born child; this one is concerned with the brain of the infant one month old. In the course of the first month of extra-uterine life the brain becomes firmer and its cyto-architecture takes on more of the adult pattern. All the characteristics of allo-cortex and iso-cortex described by von Economo in the adult brain are visible. The giant cells of the ascending frontal convolution are the most advanced, and a few formed Nissl granules are found in them. The layer of the cortex in which they lie is found to have increased more in depth since birth than any other layer. Cortical action-potentials begin to appear in this area at the age of one month.

The hypophysis

The pars nervosa.—As a result of anatomical studies E. Vazquez-Lopez (1942) has put forward a new conception of the function of the pars nervosa of the hypophysis. Nerve fibres to the hypophysis arise in nuclei of the hypothalamus, and then pass through the eminentia media of the tuber cinereum and enter the stalk grouped together in thick close-set bundles. As they enter the pars nervosa they fan out, and toward the distal portion they form a dense network of fibres running in all directions. The framework of the pars nervosa is composed of (1) its poorly developed fibrous capsule, (2) the blood vessels with their adventitial connective tissue and (3) the multitude of nerve fibres. Isolated nerve fibres leave the bundles to end in one or other of three main sites: (1) around the blood vessels, where they crowd the perivascular spaces, (2) in the pars intermedia, where a large number end in relation to blood vessels and (3) in the meningeal terminal corpuscles, which are sensory structures rich in nerve endings. All the terminal nerve fibres are very much alike in type, and are similar to perivascular sensory endings found in other parts of the body. The whole formation points to the conclusion that the pars nervosa is primarily a sensory organ, and it is suggested that it may constitute a 'chemo-receptive' or 'presso-receptive' apparatus, devoted to the reception of stimuli which enable the hypothalamic centres to control the metabolic and hormonal functions of the body.

The physiology of hearing

R. Galambos and H. Davis (1943) have studied the activity in individual fibres of the auditory nerve of the cat by means of micro-electrodes. Their results support the theory that the tone (pitch) heard depends accurately on the part of the basilar membrane of the cochlea which is excited, and that the loudness of note appreciated depends on how much of the basilar membrane is disturbed. The endings of the nerve fibres in the cochlea are imperfectly known, but it is assumed that each is in contact with a

limited number of hair cells. Galambos and Davis found that when the intensity of a sound stimulus delivered to the ear was just sufficient to excite it, each auditory nerve fibre was excited only by a narrow band of sound frequencies, and fibres were found which were specifically sensitive to such narrow bands over the range from 420 to 25,000 cycles per second. As regards its electrical activity, the auditory nerve fibre behaves in every respect like other sensory fibres; it responds to an adequate sound stimulus by a train of impulses, initially fast but gradually declining in rate. The adaptation of the latter is complete in a few tenths of a second; the rate of discharge is increased by an increase in the intensity of sound up to a maximum of 450 discharges per second. Some spontaneous activity seems to be almost constant, and excitation of the individual fibre is appreciated only by an increase of the discharges recorded. Each fibre may be said to tune in to a specific narrow band of the sound spectrum but when the intensity of the sound is increased there is a marked widening of the range of frequencies capable of exciting it, and at levels about 100 decibels above the threshold, tones as far away as three octaves below and half an octave above may be adequate for excitation. There are many nerve fibres which respond to a given frequency, and they are called in successively as the intensity of a sound is raised. The tracings suggest also that the discharges in the nerve fibre synchronize with one point in the wave cycle of the sound exciting it.

PATHOLOGY

Neural mechanisms in poliomyelitis

The mode of virus invasion.—H. A. Howe and D. Bodian (1942), in a volume published by the Commonwealth Fund, have correlated much recent work on poliomyelitis, and have described ingenious elaborations of technique by which they have been able to gain further knowledge of the method in which the virus of that disease enters and spreads and multiplies within the central nervous system. It is now clear that the former view that the virus usually reaches the central nervous system by way of the olfactory nerves is erroneous, and that in the human subject the gastro-intestinal tract in the spinal form of the disease, and the nasopharynx in the bulbar form, provide the natural portals of entry. The virus has been isolated from the faeces both of human beings and of inoculated apes, and there is evidence that it can reach the spinal cord by way of nerves innervating the gut. That the virus reaches the central nervous system by neural channels and spreads in it by the same path has been accepted since Weston Hurst's observations, and the present authors have confirmed and extended his findings. Passage takes place in the axon, but multiplication of the virus and the essential interaction between virus and nerve cell take place only in the cell body. The mesodermal and glial cellular reaction, characteristic of the lesions of poliomyelitis, is a sequel to this interaction and does not take place in the neighbourhood of cells which are not susceptible to the virus. The virus spreads in the central nervous system along fairly well defined paths, and its effects are limited to certain structures. It favours short rather than long neurones for its passage, the concentration of virus being built up in the cell stations on the routes composed of short paths. Some degree of encephalitis is a constant feature, although it is not usually clinically evident.

CLINICAL INVESTIGATION

Vestibular function

'Directional preponderance' of nystagmus in temporal lobe lesions.—Bauer and Leidler, and later de Barenne and de Kleyn also, found that after removal of one cerebral hemisphere in the rabbit there was a facilitation of induced nystagmus towards the side of the ablated hemisphere. De Kleyn and Versteegh found the same facilitation or 'directional preponderance' in human subjects suffering from unilateral cerebral lesions. G. Fitzgerald and C. S. Hallpike (1942) have continued the investigation, using an improved technique for caloric labyrinthine tests, and have found that directional preponderance of nystagmus occurs only in association with lesions of the temporal lobe. They have thus extended the work of de Kleyn and Versteegh, and have provided a new sign for the diagnosis of temporal lobe lesions. T. E. Cawthorne, G. Fitzgerald and C. S. Hallpike (1942) have applied the same technique to the examination of patients before and after unilateral labyrinthectomy performed for intractable vertigo. In all the nine cases examined there was a distinct directional preponderance of caloric nystagmus to the side upon which the operation had been

performed, but it diminished in time. The gradual return to normal suggested that there must be a bi-directional sensitivity to endolymph flow, and not merely uni-directional as postulated by Bárány, and systematic application of the caloric tests to normal subjects has confirmed that this is so.

THE ELECTROENCEPHALOGRAM

Diagnostic value of encephalography

A further year's experience can be said to have reduced positively the general estimate of the diagnostic importance, if not of the value in general, of the electroencephalogram. In the course of two years' work among soldiers in the British Army, I found electroencephalography to be of remarkably little help in doubtful cases of epilepsy, and I gradually abandoned its use as a diagnostic aid. D. Williams (1941) found that 40 per cent of epileptic patients had a normal encephalogram between seizures. Only 55 per cent of patients with known *grand mal* had abnormal encephalograms, but 90 per cent of patients with known *petit mal* and *grand mal* showed abnormal patterns in their electroencephalograms. K. H. Finley (1943), in the course of a series of tracings from 4,500 subjects representing a large variety of neuropsychiatric disorders, found that the type of rapid frequency discharge which F. A. Gibbs had designated '*grand mal* activity' was encountered in a variety of clinical conditions, and that it was met with even more often in cases of neurosyphilis and of the affective psychoses than in cases of *grand mal* epilepsy. K. H. Finley and J. B. Dynes (1942) stress the variability of the electroencephalographic tracings of epileptic patients. Eighty-six per cent of their tracings from 625 known epileptic subjects were either borderline or abnormal, but 14 per cent were normal. Many of the patterns obtained from epileptics were found in other neuropsychiatric conditions. The spike-and-wave pattern which has been usually considered typical of epilepsy occurred in less than 10 per cent of their 625 cases. The investigators concluded that the information given by the electroencephalogram was most often non-specific. Williams found abnormal electroencephalograms in 5 per cent of highly selected normal subjects (members of the Royal Air Force), in 10 per cent of less carefully selected subjects and in 26 per cent of a group of psychoneurotic patients, indicating that there is a more common constitutional abnormality in such persons than in normal subjects. As a result of several years' experience Williams has arrived at the following conclusions. (1) An abnormal electroencephalogram in an otherwise normal subject is evidence of an inborn constitutional abnormality involving the central nervous system. (2) This abnormality appears to be non-specific and may manifest itself in the subject or in his offspring as a behaviour disturbance, which may be psychoneurotic, psychopathic, psychotic or epileptic. It may be observed that the latter conclusion is in keeping with the clinical observation that psychopathic or psychoneurotic abnormalities are often present in the parents of epileptics.

NUTRITION

Vitamin E deficiency

During the past few years there have appeared numerous articles dealing with the treatment of amyotrophic lateral sclerosis and other degenerative diseases of the central nervous system by administration of vitamin E. Such studies were instigated by the supposition that chronic vitamin E deficiency in rats brought about changes in the central nervous system which were more or less comparable to those found in diseases in human beings. A. Wolf and A. M. Pappenheimer (1942) have made a critical examination of the subject and report that 'under the experimental conditions obtaining in our laboratory, lesions of the central nervous system did not occur in vitamin E deficient rats at any age'. Clinically, Fitzgerald and McArdle, and other workers have been unable to observe any beneficial effect from long-continued vitamin E therapy in cases of muscular dystrophy or of amyotrophic lateral sclerosis.

RECOVERY OF PERIPHERAL NERVES

Experimental observations on nerve union

Experimental work has been continued at Oxford by E. Gutmann, F. K. Sanders, L. Guttmann and P. B. Medawar, who, singly or in different partnerships, have published a group of papers during the year. The clinical investigations of W. B. Highet (1942, 1943) should also be mentioned. A comparison of the rate and degree of recovery after different methods of nerve union had been used was made by Gutmann and

Sanders. The peroneal nerve of the rabbit was cut in the thigh, and recovery was allowed to proceed unaided or repair was effected either by end-to-end suture or by the insertion of various types of graft.

Motor recovery.—The time of onset of motor recovery in the muscles of the small peroneus group was determined by observing the return of reflex spreading of the toes, and an estimate of the final degree of recovery attained was made by plotting the amplitude of toe spreading on an arbitrary scale. Recovery of pain sensibility in the skin of the dorsum of the foot was also studied, and the histological conditions of the various grafts were investigated—all as late as 200 days after operation. End-to-end suture gave the best results. In eight out of eight cases the animal recovered toe spreading in from fifty-six to eighty-five days. When autografts were used, eight out of ten animals showed toe spreading in from fifty-one to ninety-eight days, that is, the results were less constant but recovery when it occurred was at the same rate. When fresh grafts from other rabbits (homografts) were used, six out of seven animals recovered similarly in from seventy to 125 days. Storage of the homografts in Ringer's solution at 2° C. for seven, fourteen or twenty-one days did not cause any delay in recovery and eight out of eight animals recovered toe spreading in from sixty-one to 117 days. With dead, alcohol-fixed grafts, recovery occurred in only two out of four cases, and the times taken were 124 and 142 days respectively. Of the fourteen unaided animals only two showed recovery, the times taken being 117 and 162 days respectively. The normal amplitude of spreading was not restored after any of the procedures, and the best results were given by end-to-end suture and autografts. After 200 days autografts were histologically indistinguishable from normal peripheral stumps. Fresh and stored homografts showed some fibrosis, and alcohol-fixed nerves showed evidence of destruction and of replacement by tissues of the host. All, however, contained myelinated nerve fibres, and these were more numerous and of greater diameter in those procedures which gave the best functional results. Gutmann, using the same criteria of recovery, found that recovery of the motor function of an interrupted nerve was much more rapid after crushing than after division and end-to-end suture. The bulk of the denervated muscle begins to increase, and its threshold to direct stimulation begins to decrease, before reflex function returns, and sometimes before indirect excitability returns. After crushing of the peroneal nerve the normal weight of the muscles is nearly regained twelve weeks after the reappearance of reflex function. From a study of sixty-nine cases, the rate of advance of regeneration down the nerve after crushing is given as 2.77 ± 0.09 millimetres per day after a latent period of 18.2 days. After severance and suture regeneration proceeded at the rate of 1.69 ± 0.34 millimetres per day after a latent period of 27.7 days. Ligation of the popliteal vein and artery did not delay recovery of the muscles.

Sensory recovery.—Recovery of sensory function involves processes other than regeneration of the interrupted nerve, namely recovery of full sensation in zones of overlap and extension of fibres from these zones into the margin of the denervated area. Recovery in zones of overlap occurs generally in from two to four weeks, but in young animals it may occur within a few days. The recovery in such zones is peculiarly susceptible to various factors such as (1) local damage to the skin supplied by adjacent nerves, (2) transient block of these nerves as a result of operation and (3) all processes which tend to raise the nervous threshold such as infection, sores and advancing age. Recovery in the autonomous zone of a nerve, resulting from regeneration of the interrupted nerve, proceeds in general in a downward direction, but recovery, especially in large areas, often advances faster at the edges than in the centre, so that the analgesic area shrinks concentrically. The visible pattern of recovery, consisting in centrifugal advance and concentric shrinkage, is the same after lesions of all nerves. The nature of the lesion is of decisive importance for the rate and ultimate degree of restoration of function; after division and end-to-end suture recovery is slower, more irregular and less complete than after crushing; crushing of the nerve over a length of four centimetres delays the recovery, and the eventual recovery of function is less complete than after a single local crush. Study of the time of recovery after production of lesions at different levels gives estimates of the rate of progress of functional restoration down the nerve as follows: 3.35 millimetres per day (with a latent period of twenty-two days) after crushing and 2.46 millimetres per day (with a latent period of forty days) after division and suture. These rates of advance of restoration of function are higher than those obtained by the study of motor function, and it is evident that there may be

various reasons for the differences of rate observed. The margin of algesia, as observed on the dorsum of the foot in seventeen animals, advanced, on the average, at a rate of 1.98 ± 0.09 millimetre per day when the nerve had been crushed and 1.57 ± 0.15 millimetre per day in six cases in which the nerve had been cut and sutured. The rate of advance of the margin of algesia was higher (2.3 millimetres per day) when the nerve had been crushed near the ankle than when it had been crushed in the thigh (1.8 millimetre per day).

Neuroma formation

Methods of prevention.—L. Guttman and P. B. Medawar (1942) have studied the formation of neuromas on nerve stumps, and methods of preventing them. Neuroma formation and the development of strong adhesions between the stump of a nerve and its bed do not occur in the absence of regenerating nerve fibres, so that the problem is one of the inhibition of fibre regeneration. This may be accomplished by thorough treatment of the terminal stretch of the nerve with suitable tissue fixatives. An attempt was made to evaluate various chemical methods of inhibition by a series of injections of fixatives and non-fixatives, under uniform conditions, into the tibial nerves of rabbits. The reagents of which the effects were investigated were alcohol, tannic acid, formaldehyde (10 per cent, 20 per cent and 40 per cent) and gentian violet among fixatives, and quinine hydrochloride, optochin (aethylhydrocupreina), antipyrin, sodium taurocholate, beryllium nitrate, crotonaldehyde and heptylaldehyde among non-fixatives. The results clearly distinguished formaldehyde and gentian violet by their successful effect from the other fixatives, and distinguished fixatives as a class from non-fixatives. Formaldehyde in concentration of 20 per cent and upwards and a 1 per cent solution of gentian violet prevent the formation of end-bulbs and the development of adhesions between the nerve and its bed for at least a year. Alcohol is effective only for periods of less than two months. Other fixatives occupy an intermediate position.

In the practical application of the above results certain precautions must be observed. Thorough permeation of the nerve by the solution is essential; injection should be both of intraneural and subepineural type. Steps should be taken to control the distance which the injected fluid may travel up the nerve, for example by a light ligature applied some centimetres below the lowest working branch of the nerve. The fluid should be coloured; methylene blue may be added to a formaldehyde solution. There is always a danger of leakage of the fluid from the nerve after injection, and therefore the nerve should be replaced in such a position that leaking fluid can do little harm. In no case should the treated nerve be left in contact with another nerve.

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DISEASES OF THE PROSTATE GLAND AND BLADDER

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DISEASES OF THE PROSTATE GLAND

Treatment of benign enlargement of the prostate gland

Surgical treatment: perurethral resection.—This method of treatment now has an important place in the treatment of the obstructing prostate gland, and there are few, if any, urologists who deny its usefulness. But a survey of the statistics of the various clinics of Europe and of the United States of America shows that the frequency with which the perurethral approach is employed varies greatly. In the Mayo clinics at Rochester, Minnesota, it has practically taken the place of prostatectomy, but in some hospitals, both in Great Britain and abroad, it is still regarded as a method to be used only in exceptional cases. In spite of these wide variations the indications for perurethral resection have been more clearly defined during the last few years.

Indications for surgical treatment.—Operations on the prostate gland are required primarily for the relief of obstruction, and the chief indication for operation is the presence of increasing residual urine. Residual urine of itself is not harmful, but the complications likely to arise from its presence may be very serious, chief amongst these is the effect on renal function. If the volume of residual urine should rise beyond a certain level—and no figure indicating the danger-point can be given—the work of the kidney becomes embarrassed. Most surgeons therefore advise operative interference if there is a constant residuum of five or more ounces. Another danger that arises from the presence of residual urine is infection; if this occurs it is unlikely that medical treatment alone will ever produce a permanent cure when the bladder is imperfectly drained. The onset of acute cystitis usually causes a temporary decrease in the quantity of residual urine, the initial fall giving place to a rise when the infection has become chronic. Another indication for operative interference is the observation through the cystoscope of signs of bladder stress such as saccululation and marked trabeculation. These signs indicate that the obstruction is having an injurious effect on the bladder wall and that, if irreparable damage is to be prevented, relief must be given. Improvement in technique has extended the scope of perurethral resection, but in Great Britain the majority of urologists believe that even so it should not be regarded as being a substitute for enucleation. Resection is a method of treatment for certain patients and for use in special circumstances. Broadly speaking, the special patients are those in which the prostate gland is not very large, although the obstruction it causes may be great; the special circumstances are those in which for some reason or other, for example the poor state of the patient, a total enucleation is contra-indicated on account of the risk which it entails.

Technique of resection.—The method of resection and the instrument employed vary with different surgeons, but in Great Britain the McCarthy operation is the most popular method. A number of modifications of the original McCarthy resectotome have been introduced, the one adopted by me being that devised by R. O. Ward. In this instrument an inclined plane has been built into the beak of the resectotome, and this has the effect of pushing forward the loop as the latter is advanced from within the sheath to the extreme forward position. A modification such as this not only keeps the loop in the centre of the optical field but allows it to be thrust into the tissues at the moment when the diathermy current is turned on. Ward has pointed out that when the field of operation is examined after a prostate gland has been enucleated, a cavity is found which narrows below and above, at the points at which it communicates with the urethra and the bladder respectively. Ward's aim is to reproduce by means of a resectotome a condition similar to that found after an enucleation. He therefore advocates the carrying out of what may be called a subvesical resection. To perform this type of resection the cutting loop actually enters the bladder only in the mid-

posterior line of the vesical outlet ('6 o'clock'). Laterally it digs into the prostatic tissue on the urethral side of the internal meatus, forming a cavity similar to that left by enucleation. This method of operation avoids the danger of damaging the trigone and the still greater danger of opening up the subtrigonal tissues. One of the most serious post-operative complications of the earlier techniques of resection was prolonged post-operative sepsis, which in many cases was due to infection of the pelvic cellular tissues. Opening up the cellular tissues is especially liable to occur when deep cuts are made laterally with the loop, or when they are made toward the anterior segment of the vesical outlet. In these situations there is less prostatic tissue between the instrument and the pelvic fascia.

Another recent improvement has been the fitting of a Bigelow's evacuator to the resectotome, which allows the removal of portions of prostatic tissue which have fallen into the bladder. Perurethral drainage has also been rendered more comfortable for the patient by the substitution of a Foley's catheter for the ordinary tied-in gum-elastic catheter. In this ingenious catheter there is below the eyelet a rubber bag which, when collapsed, is not visible but which, after the catheter has entered the bladder, can be distended with air or fluid: The distending bag rests lightly on the neck of the bladder and obviates the necessity for securing the catheter in position by tapes or by strapping. Being a soft instrument it can be retained even for a fortnight without causing discomfort or undue irritation of the urethra. It is equally useful for either pre-operative or post-operative drainage. During the post-operative period sepsis is prevented by frequent bladder irrigations and by means of sulphanilamide therapy.

Endocrine treatment of benign enlargement of the prostate gland.—The work of A. Lacassagne (1933), of H. Burrows and N. M. Kennaway (1934) and of A. S. Parkes and S. Zuckerman (1935), which showed that enlargement of the prostate gland could be produced in animals by giving repeated doses of oestrin, encouraged the belief that prostatic enlargement in human beings might eventually prove amenable to endocrine therapy. This belief gained support when K. David, J. Freud and S. L. de Jongh (1934) proved that the action of oestrin on the prostate gland could be inhibited by injections of testosterone, and when Parkes and Zuckerman, working with monkeys, confirmed the findings of de Jongh and his colleagues. There therefore existed plenty of experimental support for an attempt to treat prostatic enlargement in human beings directly by injections of male hormone, or indirectly by the use of gonadotrophic substances. But sufficient time has now elapsed to show that any early hopes have not been realized and that the endocrine treatment of prostatic enlargement is a failure. Members of a special committee of the Medical Research Council treated patients with prostatic enlargement by means of injections of 50 milligrams of testosterone given twice a week. The patients were carefully examined before and after a three months' course of injections and in order to make the test more conclusive and to exclude psychological factors, half of the ampoules supplied to those engaged in the research contained sesame oil only, and no testosterone. When the results of the investigation were reported it was found that in no case was there any objective proof of improvement as indicated by a reduction in the size of the prostate gland or in the quantity of residual urine, even although some of the patients declared that they felt better. The results were therefore completely negative. It must be borne in mind that the symptoms of prostatic obstruction fluctuate in any one patient, sometimes being in abeyance and at other times increasing in severity. Great care, therefore, must be taken before it is concluded that improvement is actually due to any treatment which may have been given. It is interesting to note that P. J. Kahle and E. Maltry (1940) have claimed that beneficial effects have been produced in cases of innocent enlargement of the prostate gland from what might be termed the 'opposite' form of treatment, namely the injection of female hormone, stilboestrol, and yet on theoretical grounds treatment of this kind should have increased rather than diminished a patient's discomfort.

TREATMENT OF MALIGNANT DISEASE (CARCINOMA) OF THE PROSTATE GLAND

By stilboestrol

Long ago F. G. Hopkins pointed out that cancer-producing substances, namely oils and tars, although they differ in detail from arc nevertheless akin to some of the substances which occur naturally in the body, for instance the hormones which control certain functions of sex. He suggested that the subjection of a patient to pro-

onged administration of a sex hormone might even encourage the growth of glandular cancer. It is known that the anterior lobe of the pituitary gland contains two hormones, one which is secreted by the eosinophil cells and is concerned with growth, the other by the basophil cells which are associated with sexual development. These two hormones are antagonistic to each other, the growth hormone counteracting the effect of the sex hormone if both are injected simultaneously. A new form of endocrine therapy, based on the above facts, has been instituted for patients with primary or secondary carcinoma of the prostate gland, namely treatment by stilboestrol.

Clinical results.—P. J. Kahle, H. D. Ogden, Jun. and P. L. Getzoff (1942) report striking results from injections of stilboestrol. In every instance this method of therapy brought about immediate relief of pain and of micturition symptoms in sufferers from primary malignant disease of the prostate. Two out of the six patients treated had very advanced lesions and were even bedridden. Both of these patients were restored to activity in four and six weeks respectively after the beginning of treatment. The size and consistency of the primary growth were favourably affected and a regression was noted in metastases. The microscopical examination of prostatic tissue obtained by means of a resectotome before and after treatment showed regressive changes in the nucleus and in the cytoplasm of the malignant cells. The stilboestrol was given in the form of daily intramuscular injections, seventy injections of 5 milligrams each being given and then 153 injections of 1 milligram each. Ill effects were not observed as a result of the treatment, except in one case—that of a transient gynaecomastia. R. D. Herrold (1941) has also reported an improvement after oral administration of stilboestrol in the clinical condition of patients with carcinoma of the prostate gland. Although the number of patients treated by this method is still small, the results obtained are encouraging. At the present time the best treatment available for patients with malignant disease of the prostate gland appears to be resection for the relief of obstruction, with a subsequent course of injections of stilboestrol.

By castration

Clinical results.—This is now advocated as an alternative to treatment by stilboestrol. C. Huggins, R. E. Stevens, Jun. and C. V. Hodges (1941) report that in nineteen of twenty-one cases of advanced prostatic carcinoma, castration caused shrinkage of the prostate gland and a general improvement in the condition of the patient. The only unfavourable effects noted from the castration were the occurrence of hot flushes and sometimes a temporary swelling of the ankles. C. R. Marquardt and W. A. Flaherty (1942) report that eleven out of nineteen patients were benefited by this type of treatment. Other observers have suggested that when relief is obtained from deep X-ray therapy, it may well be due to an indirect action on the Leydig cells of the testis. So far none of those who have used castration for the treatment of prostatic carcinoma has reported that it has given rise to psychological disturbances, but nevertheless it must be remembered that it was for such a reason that castration was abandoned as a method of treatment in cases of prostatic enlargement in pre-prostatectomy days.

COMMENTARY

Many British urologists have reported favourably on both these methods of treating carcinoma of the prostate. I have seen advanced cases with secondary deposits, cachexia and pain quickly respond to either stilboestrol or castration; pain has disappeared, the general condition has noticeably improved and some patients who were bedridden have been able to get up. It is by far the most hopeful line of treatment of malignant disease of the prostate which has yet been evolved. The ideal method of dealing with prostatic carcinoma is a resection of the prostate combined with castration or with stilboestrol injections.

HUNNER'S ULCER OF THE BLADDER

Clinical picture and diagnosis

C. C. Higgins (1941) states that the symptoms of this troublesome disease are remarkably constant and that frequency of micturition both by day and by night is the most characteristic complaint. Freedom from symptoms at night is a sure sign that the condition is not Hunner's ulcer. The next most constant symptom is suprapubic pain. Again, some 60 per cent of patients suffering from Hunner's ulcer have haematuria and 60 per cent have pyuria. In 100 cases reviewed by Higgins, 90 per cent were females and only 10 per cent were males. The average age of the patients was forty-eight years.

Cystoscopy.—It is often difficult to detect the ulcer, especially as distension of the bladder is painful. To overcome this spinal anaesthesia is helpful. The commonest situation for the lesion is the apex, or dome, of the bladder, and the most characteristic appearance is a small area of granulations which bleed readily. The surface of the ulcer is generally clean and is never, like many other forms of bladder ulcerations, covered with phosphates. The ulcer is usually single, but multiple areas of ulceration sometimes occur.

Treatment

In the less serious cases the lesion often yields to fulguration combined with repeated distension. T. L. Pool and J. L. Crenshaw (1941), working at the Mayo Clinic, start treatment with a one in 5,000 solution of silver nitrate. After the bladder has been thoroughly irrigated a few ounces of the solution is left in the bladder for five minutes and is then evacuated by means of a catheter. The strength of the solution is gradually increased up to a maximum of 1 per cent. E. Davis (1941) prefers instillations of methyl violet. In a few serious cases in which the bladder capacity has been markedly reduced and in which pain and frequency make life intolerable, transplantation of the ureters into the bowel must be undertaken.

ADVANCED TUBERCULOSIS OF THE BLADDER

Treatment

What can be done to relieve the condition of the patient in the later stages of tuberculosis of the urinary tract? Sympathectomy has given very varied results and, even if it relieved pain, it would not solve the other problems resulting from the existence of a small contracted bladder, from incompetent uretero-vesical valves and from strictures of the lower parts of the ureters and of the urethra. The only possible way of dealing with these complications is to use some method of diverting the urine from the bladder.

Surgical procedures.—The three usual methods of short-circuiting the bladder are by nephrostomy, uretero-enterostomy and cutaneous ureterostomy. The first of these three methods is unsuited to the treatment of the particular complications under consideration because, unless nephrostomy is associated with ligation of the ureters, it does not prevent some urine from reaching the bladder. Transplantation of the ureters into the bowel has a high mortality rate, owing to the diseased state of the ureters and to the poor condition of the patient. For these reasons cutaneous ureterostomy is the treatment best suited to the patient in the later stages of urinary tuberculosis. The operation is comparatively simple. The ureter is exposed through an iliac incision and is dissected from the peritoneal and the retroperitoneal tissues, care being taken to avoid damage to its blood supply. The vesical end is clamped, divided and carbolized, and the clamped ureter is brought to the surface so that it lies in a slight curve between the renal pelvis and the skin, without tension or angulation. The abdominal wound is then closed without drainage, a length of several centimetres of ureter being left protruding from it. Sutures are not used to anchor the ureter to the muscles or fascia because they are apt to cause narrowing or interference with its blood supply. Fixation is obtained by splitting the exposed ureter and by turning down the flaps to meet the edges of the skin incision. Urine is diverted from the wound by passing a rubber catheter up the ureter to the renal pelvis. After healing of the wound the patient's abdominal wall is kept dry either by means of catheters or else by the use of an apparatus similar in construction to a colostomy bag.

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TROPICAL MEDICINE

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MALARIA

Incidence and prevention

Regional preventive measures.—Much of the vast literature on this most widely distributed disease is of local interest, but researches in the war areas are important. Thus E. Collignon (1940) records that in Algiers in 1939 an epidemic of malignant tertian malaria followed abnormally heavy rainfall such as appears to have occurred in 1943. Control measures gave good results, but they should have been extended and intensified. In Bulgaria, where fighting may again take place, K. Drensky (1940) reports that malaria is most prevalent along the Danube and the Maritza and Struma rivers; our troops suffered severely there from the disease in the war of 1914–18. In the above area varieties of *Anopheles maculipennis* are the carriers; the spleen index reaches from 81 to 100 per cent in the autumn, and blackwater fever occurs. During the last ten years Rockefeller Foundation workers have been testing preventive measures in this area, beginning with the free prophylactic issue of quinine; only limited benefits were obtained. Later they found that a systematic campaign against the breeding of anopheles larvae, with drainage, the destruction of breeding-places and cleaning of streets as its weapons, furnished an extremely effective and cheap method of converting a heavily infected region into a healthy one. The number of anopheles in houses and stables, the spleen and parasite rates and the number of new cases were greatly diminished; the previously high spleen indices of from 90 to 95 per cent, and the parasite indices of from 60 to 75 per cent were reduced. How far such measures will prove to be practicable under the more mobile conditions of the present war remains to be seen.

Palestine is another military area in which remarkable antimalarial work is reported on in a Review (1942) by the Department of Public Health. The most malarious area extends along the whole length of the Jordan valley, especially where seepage occurs at the foot of the mountains, which is favoured by heavy spring rains. The domestic *A. bifurcatus*, which breeds in wells and cisterns, is responsible for nearly all the urban malaria, and *A. elutus*, an inhabitant of stagnant pools, wells and swamps, for the malaria of rural areas. Mosquito control in Palestine has been essentially of anti-larval character; in towns it consisted in the mosquito-proofing of wells and cisterns and in the closing of unnecessary wells, with the result that by 1925 urban malaria was under control; the spleen rate in Jerusalem had fallen from 44·3 to 5·7, and attendances of malarial patients at dispensaries had been reduced from 7·2 to 0·5 per cent of the population. In rural areas reliance was placed on drainage and irrigation schemes, combined with a system of filling up pools or drying them up by pumping operations; a good spring cleaning was also carried out before the onset of the malarial season. Reclamation and cultivation of land has also helped. Energetic cooperation of the people was secured, with the result that the successful antimalarial measures have cost only 1½d. per head of population per annum—a low expenditure that should be within the reach of the poorest countries.

Recent antimalarial work in India has been dealt with by S. R. Christophers (1943), who points out that New Delhi was built on a healthy site after the first site selected had been given up, a malarial survey having shown it to be very unhealthy. The rural conditions, under which 90 per cent of the Indian population live, present more difficult problems than do urban ones, but the workers in the Malarial Institute of India, and in the Ross Institute in Assam, are gradually evolving the best methods of dealing with them. Assam is now an important base for military operations in Burma, and researches have led to the adoption of the plan of limiting the breeding of the carrier, *A. minimus*, in watercourses by planting selected shade-producing plants along them, and by flushing the streams intermittently by means of automatic apparatus to wash away the breeding larvae. D. K. Viswanathan records the practical results of ten years' work in Assam in both urban and rural areas, which show great reduction in both the spleen and parasite indices. On the other hand, R. C. M. Thomson (1941)

advises the use in Assam of a simple anti-larval measure, namely the removal of the grassy edge of the streams in order to expose the bare banks to sunlight.

A noteworthy triumph, due to the use of biological methods by the Rockefeller Foundation, is reported from Brazil by R. B. Fosdick (1941). In *Surveys and Abstracts* 1940, I recorded the serious epidemics of malaria in Brazil which broke out after the introduction by ship of the dangerous West African malarial carrier, *A. gambiae*. It has now been reported by Fosdick that, as the result of a great effort by more than 2,000 trained workers to eradicate this carrier from the extensive areas of Brazil over which it had spread, thorough search during 1941 failed to show a single specimen. Watchful care will be required to prevent its reintroduction; for instance a dead specimen was recently found in a fumigated airplane. A point of theoretical interest so far has been made by H. E. Shortt and K. P. Menon (1940), in the successful infection of *Macacus rhesus* and of fowls with *Plasmodium knowlesi* by allowing heavily infected blood to drop into their uninjured mouths.

Treatment

Since 90 per cent of the world output of quinine in the Dutch East Indies fell under the control of Japan, the power of the United Nations to wage successful war in the Near and Far East largely depends upon the employment of atebirin (mepacrine hydrochloride). F. Meythaler (1942) advises that the drug should be given in the usual daily amount of 0.3 gramme (5 grains) in benign tertian cases but that, in all except the mildest cases of malignant tertian infection, the daily dose should be doubled during the febrile stage, or atebirin musonate (mepacrine methanesulphonate) should be given intramuscularly daily in 0.3 gramme doses dissolved in 10 cubic centimetres of distilled water. In pernicious cases he recommends, in addition, slowly injected intravenous doses of 0.5 gramme (8 grains) dissolved in 20 cubic centimetres of a 10 per cent solution of glucose once or twice daily. In malignant tertian cases in East Africa J. Bryant (1942) found it necessary to give from 0.6 to 0.9 gramme (10 to 14 grains) of atebirin daily, with plenty of hot sweet tea or sugar in some other form; he did not see any ill effects from such doses.

KALA-AZAR

Aetiology

Transmission by Phlebotomus argentipes.—The outstanding event in tropical medicine during 1942 was that the final proof was provided that the infection of kala-azar is conveyed to human beings through the bites of *Phlebotomus argentipes*; this has been established nearly forty years after the human stage of the *Leishmania donovani* was discovered (1903). Actually the latter was cultivated *in vitro*—with the discovery of the flagellate stage—in 1904 by myself, and I suggested the bedbug as a possible carrier. In 1907, the finding by W. S. Patton of a few flagellate forms in the gut of bedbugs fed on patients with kala-azar, lent some support to that hypothesis, but no further advance was made until team-work in the then recently opened School of Tropical Medicine at Calcutta enabled L. E. Napier and R. B. Lloyd in 1924–5 to furnish epidemiological evidence pointing to the sand-fly, *P. argentipes*, as the probable carrier of the infective organisms. R. Knowles, L. E. Napier and R. O. A. Smith (1924) soon afterwards demonstrated the common and extensive development of the flagellate stage of the organisms in the alimentary canal of such sand-flies several days after the latter had been fed on kala-azar patients; these observations were soon confirmed by others, who reported extensive involvement of the mouth parts of the insects. Attempts to infect human beings by means of sand-flies fed in such a way, which had become justifiable since the establishment of the remarkable curative effect of antimony salts in kala-azar, failed, however, and the occasional successful transmission of the disease to hamsters, after very long incubation periods, was not conclusive. Success has at length been obtained in five consecutive feeding experiments on Khasia Hill men in Shillong who had not resided in a kala-azar infected area; the experiments were carried out by C. S. Swaminath, H. E. Shortt and L. A. P. Anderson (1942) who adopted the simple technical modification of keeping alive *P. argentipes* organisms fed on kala-azar patients, by subsequently feeding them on raisins instead of giving them blood feeds. Repeated feeds on the Khasias were given over from three to five months before the men were shown to be infected, so that the precise incubation period of the disease is not settled. The authors suggest that their success may have been due in part to the fact that the sand-flies were fed on patients with the epidemic form of the disease

met with during a recrudescence in Assam; they think this may have resulted in increased virulence of the parasite.

An inquiry by R. O. A. Smith and I. Ahmed (1941) into the prevalence of malaria and of kala-azar in the Bihar province of India, immediately to the west of Bengal, has led them to the conclusion that the sudden increase in the number of cases in that area is probably the result of lowered resistance brought about by attacks of malaria. This observation confirms my finding in 1897 that the original great epidemic of kala-azar in Assam, starting in the Garo Hill district, was due to epidemic malaria which had prevailed for several years in the adjoining Bengal districts of Dinajpur and Rungpur, in the north-west of which area I found a focus of endemic kala-azar still remaining in 1904. Smith and Ahmed add that attacks on the adult sand-flies in houses is more likely to be successful as a preventive measure than an attack on the larval stage of these insect carriers. The occurrence of thirty cases of kala-azar with twelve deaths, in a battalion of the King's African Rifles in Kenya, has been reported by A. C. E. Cole (1942). Only tartar emetic was available for treatment and some fatal relapses occurred.

Treatment

M. H. Sati (1942) advises the alternate use, for a week at a time, of tartar emetic and a pentavalent antimony compound with which he obtained favourable results. The beneficial effects of the use of stilbamidine (4:4'-diamidinostilbene) in cases of kala-azar have been confirmed by L. E. Napier, P. C. Sen Gupta and G. N. Sen (1942), who conclude, from experience of 100 cases, that the introduction of this preparation is a very great advance even on the use of neostibosan; moreover, patients who are antimony-resistant respond to it. The dosage the above workers finally adopted was an initial dose of 0.025 gramme ($\frac{2}{5}$ grain), increased by 0.012 gramme ($\frac{1}{5}$ grain) at a time, up to a maximum of 0.001 gramme ($\frac{1}{100}$ grain) per pound of body weight. Reactions in the form of unpleasant sensations and of low blood pressure are controlled by a previous injection of adrenaline, and are not dangerous. Although many of the patients were in an advanced state of the disease, only 2 per cent died and another 2 per cent relapsed. J. D. Fulton and W. Yorke (1942) found increased toxicity in old solutions of stilbamidine, and therefore they advise that only freshly made solutions should be used.

TYPHUS FEVER

In the first three months of 1942 a marked increase of the disease in Algeria, in Morocco, in Tunisia and in Roumania, and continued prevalence in Germany, Hungary and Spain were recorded (*Public Health Reports*, 1942¹). The League of Nations Health Section gave data for the second quarter of 1942 recording 1,270 cases in Germany and Hungary, so there is apparently not any lack of sources from which epidemics may arise in Europe in the more dangerous post-war period, when communications will have been reopened. At the end of 1942 in North Africa, typhus fever was reported to be spreading rapidly in the departments of Algeria, Oran and Constantine, with 2,148 cases notified within the first three weeks of the year (*Public Health Reports*, 1942²). Several hundred cases have also been recorded in Morocco and in Tunisia, all the incidence rates being higher than in preceding periods.

The transmission of typhus fever infection, by the blood of a donor who proved to be in the incubation period of the disease, has been reported by E. Dormanns and E. Emminger (1942). The serial infection of laboratory workers through droplets from the lungs of infected mice is reported by W. Löffler and H. Mooser (1942), who note that previous inoculation of such workers with vaccines greatly reduced the severity of the induced attacks. Prophylactic inoculation should, therefore, be performed in the case of those persons in contact with the disease, including hospital and laboratory workers. M. van den Ende, E. H. R. Harries, C. H. Stuart-Harris, A. J. Steigman and R. Cruickshank (1943) confirm the soundness of such advice, since they record that no deaths occurred among twelve previously vaccinated laboratory workers who were infected by droplets, although three of them were in the dangerous age category of forty-five years and upwards.

'Typhus endemic index' is a term applied by G. Seiffert (1942) to the percentage of at least 50 persons (children being the best subjects for the investigation), in whom reactions to *Proteus OX19* were obtained in dilutions of 1 in 100 and over. An index of 16 in a group of Russian prisoners showed the presence of the disease, by permitting the diagnosis among them of some unsuspected mild cases of typhus fever which were

of epidemiological importance. A simple bedside diagnostic agglutination test has been described by W. Steuer (1942). From a drop of free-flowing blood from the ear, three small droplets are spread with a platinum loop on a slide, and 0.02, 0.04 and 0.08 cubic centimetre respectively of a killed suspension of *Proteus OX19* is added to the drops of dried blood and is mixed with them. The formation of sparse granules or of greyish-white floccules at the end of one, five and ten minutes is noted under a microscope in which a lens with low magnification is used. Comparisons with the results obtained with standard dilutions enable evaluations to be made.

Treatment

A reliable treatment for typhus fever is still lacking. P. Durand and L. Balozet (1941) report on a trial of a serum made by inoculation of horses with *Rickettsiae* from the lungs of mice infected by the intratracheal route; this they found to be more effective than the serum obtained from convalescent patients. The death rate in treated patients was 4.48 per cent in 112 indigenous cases in Tunisia, against 14.28 per cent in 140 controls, but the former may have comprised rather milder and earlier cases.

Complications other than pulmonary lesions were less common and pronounced amelioration of the symptoms was noted. The need for further trials is indicated. Beneficial results are claimed by van Meerendonk (1942) from the administration of atebirin and plasmoquine, with reduction in the duration of the fever and with recovery of seven patients, aged from forty-two to forty-nine years. The atebirin (mepacrine) was given in doses of 0.06 gramme (1 grain) thrice daily, and plasmoquine (pamaquin) 0.02 gramme ($\frac{1}{2}$ grain) was given once a day. When broncho-pneumonia occurred as a complication it nearly always yielded to the intravenous injection of sulphapyridine.

YELLOW FEVER

Distribution

Further investigations by T. P. Hughes, H. R. Jacobs and A. W. Burke (1942), of the incidence of yellow fever in Uganda show that this disease is at present confined to the areas bordering on the Sudan and the eastern Belgian Congo. In the latter area as many as from 8.9 to 22.6 per cent of those persons tested showed serum immunization; this indicates the presence of a persisting yellow fever infection; a strain of the virus has been isolated from one of two patients with clinical evidence of the disease.

Prophylaxis

The continued success of Rockefeller campaigns against yellow fever in North and South America has been recorded by W. A. Sawyer (1942). The outbreaks of urban yellow fever transmitted by *Aedes aegypti* have been absent everywhere, and only in South America is the jungle type present. Breeding of the carrier mosquito in cities has been so greatly reduced that in many the cost of the service has been lowered. The danger persists of the jungle type reaching cities, and vaccinations on a large scale against that form of the disease remain the most effective method of control. A further advance in the campaign for prevention has been reported by R. B. Fosdick (1942), who records the discovery of the carrier of the jungle form in a tree-top breeding mosquito. This explains the prevalence of the disease in foresters engaged in felling trees, and it also explains the way in which the virus may be carried over from one rainy season to another. The successful simultaneous use of vaccines against smallpox and yellow fever, in which the usual scarification method was adopted, has been reported from Senegal by M. Peltier, C. Durieux, H. Jonchère and E. Arquie (1940). Serum tests showed 95 per cent of protections, which lasted for at least a year, against yellow fever; the method of immunization is being extended to other areas of West Africa. On the other hand, outbreaks of jaundice in the American Army after large-scale inoculations against yellow fever, and in Brazil have been reported by J. P. Fox, C. Manso, H. A. Penna and M. Para (1942). In the American Army, cases occurred after an incubation period of from forty to 120 days, with a fatality rate of 0.2 per cent, but it was not a form of yellow fever, as it occurred in those who had become immune to that disease. It is believed that the risk of jaundice has been eliminated by the omission of the use of human serum in carrying out the preventive inoculations.

TRYPANOSOMIASIS

Clinical picture

Congenital trypanosomiasis.—Two cases of hereditary trypanosomiasis, said to be the first to be indubitably established, have been reported from the French Cameroons

by David and Pape (1942). The parasite was demonstrated immediately after delivery in the blood of the mother, of the infant and of the umbilical cord.

Treatment

A new arsenical preparation called azo-arsenobenzene, which had given promising results in laboratory animals, has been reported on by E. A. H. Friedheim (1941). It has the unusual property for organic arsenical compounds of being able to traverse animal membranes, and is stable in the air and in solution for six months at from 18° to 20° C., but not at 37° C. Six hours after intravenous injection the drug can be found in the cerebrospinal fluid. The author used it in cases of West African sleeping sickness, in doses of 0.5 gramme (8 grains) in a 5 per cent watery solution, repeated from eight to twelve times at intervals of two or three days. Only the immediate results in forty-one cases are at present available, and in thirty-one patients the trypanosomes disappeared from the blood and from the glands after the first dose. The drug is well tolerated and ocular lesions did not occur after its use. In the Cameroons M. Vaucel (1941) reports that a treatment campaign reduced the 54,712 new cases found in 1927-8 to only 6,000 in 1929; since then the number has been stationary. On the Gold Coast G. F. T. Saunders (1941) has tried 4:4'-diamidinodiphenoxypentane (pentamidine) in fourteen cases of sleeping sickness, with promising results. Four injections sterilized the peripheral blood in four days, and seven out of ten patients with involvement of the central nervous system were possibly cured; untoward effects were negligible.

CHOLERA

Prevention

Serological identification.—In India and in the Far East, protective inoculation of our troops against cholera is of great importance; the first essential measure is the identification of the particular causal vibrio, recent progress in the serological identification of which has been well summarized by J. Taylor (1941). The most important conclusion is that 'the incidence of vibrios inagglutinable with O group I (Inaba strain) serum in cases of clinical cholera in Calcutta would appear to be no greater than in the general population of the area'. Thus other vibrios, including the much discussed El Tor type, are intestinal inhabitants as often in non-cholera as in cholera subjects, and only the above-mentioned strain is the causal organism of the disease. Further the 'carrier', such as is known in the case of typhoid fever, does not exist in the case of cholera, in which disease convalescent patients are generally free from the causal vibrio five days after the onset of the attack; the vibrio exists in water for a maximum of only sixteen days, and it has not been isolated except in direct connexion with a cholera case.

Treatment

Hypertonic salines.—Pyrogen-free hypertonic salines for intravenous use in cholera have been prepared by G. Panja, K. S. Malik, B. M. Paul and S. K. Ghosh (1942), by redistilling distilled water in an all-glass still, a few drops of sulphuric acid being added in order to make the solution faintly acid to litmus paper, and a few crystals of potassium permanganate to give the mixture a faint pink colour throughout the process. Rigors and high temperatures are much diminished by the use of the above preparation, and it can be administered safely to patients with a high rectal temperature. C. Tui and A. M. Wright (1942), who describe the equipment used, have dealt with the same difficulty by filtering the solutions through specially compressed asbestos pads; these are effective in filtering crystalloids such as sodium chloride, dextrose and sodium citrate, but not colloidal preparations such as serums and gum acacia.

Sulphaguanidine.—The success of sulphaguanidine in the treatment of bacillary dysentery led R. N. Chopra, A. J. H. de Monte, S. K. Gupta and B. C. Chatterji (1941) to try the drug in cases of cholera, in an initial dose of 1 gramme (15 grains) with subsequent doses of 0.5 gramme (8 grains) every six hours for seventy-two hours. The mortality in a series of 218 cases was 3.21 per cent, against 6.38 per cent in ninety-four controls. The drug is non-toxic and the patients receiving it passed fewer stools and required less intravenous saline.

BACILLARY DYSENTERY

Treatment

Hypertonic saline transfusions.—This disease is especially likely to become prevalent under war conditions, so that the following observations will be of value. A tendency to hypochloraemia in patients with bacillary dysentery has been pointed out

by G. Walther and L. Gunther (1942); this indicates the use of hypertonic salines which was first advised by me. The present authors recommend intravenous injections of from 10 to 20 per cent saline in quantities of from 20 to 40 cubic centimetres. L. T. Poole (1942) points out that the refined and standardized Army anti-Shiga serum contains 50,000 international units in less than 10 cubic centimetres; this is sufficient for an initial intravenous dose even in fulminating cases.

Sulphaguanidine.—Several workers have confirmed the value of sulphaguanidine in bacillary dysentery. Thus N. H. Fairley and J. K. S. Boyd (1943), with an experience of over 500 bacteriologically proved cases, regard the drug as a specific in both the acute and chronic stages, on account of its bacterioscopic action which is complementary to that of Shiga antitoxic serums. They advise an initial dose of 0.1 gramme ($1\frac{1}{2}$ grain) per kilogram of body weight, and afterwards half that dose given four-hourly for as long as the stools exceed five daily, and the same dose given eight-hourly until the stools remain normal for two days. E. Bulmer and W. M. Priest (1942) also found the drug to be specific in primary cases of dysentery in the Middle East.

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VENEREAL DISEASES

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INCIDENCE

In civil practice and in the Forces

The increase in the incidence of venereal diseases in England and Wales, which was reported in Medical Progress (Critical Survey section) 1943, p. 87, has continued, and in 1942 the number of new cases of early syphilis was approximately 120 per cent greater than that in 1939. It should be remembered, however, that this increase was on a remarkably small number of cases (less than 5,000) dealt with in the earlier year. The greatest increase has occurred at seaports, as might be expected, having regard to the chances in such areas of importation from other—more heavily infected—countries. As regards gonorrhoea, the figures derived from the treatment centres are an unreliable index of incidence, owing to the far greater tendency of the general public to resort for treatment to private practitioners. From the ratios of gonorrhoea to syphilis prevailing in the Forces, in which practically all cases come to notice, I should judge that the general incidence of gonorrhoea in Great Britain was now between six and seven times that of syphilis, but the returns from the civil treatment centres show that the ratio of syphilis to gonorrhoea is much greater in the ports than in the inland towns. This suggests that syphilis is increasing at a greater rate in the ports.

COMPULSORY TREATMENT

Under the terms of Regulation 33B of the Defence (General) Regulations, 1939, which became law on the 5th of November, 1942, if a 'special practitioner' (practically a venerologist), as defined in the Regulation, receives from a patient with syphilis, gonorrhoea or soft chancre identifying particulars of the person supposed to be responsible for the infection (termed the 'contact'), he must send a special form containing such information (Form 1) to the medical officer of health of the county or county borough in which the contact is believed to reside. If the medical officer of health receives two or more such forms respecting different patients but naming the same contact, he can require the latter to undergo examination and any necessary treatment until he or she is pronounced non-infective; he is recommended, however, to try first the effect of persuasion, and to serve the necessary form (Form 2) on the contact only when it is clear that the latter will not attend voluntarily for treatment. The Regulation, besides bringing under control irresponsible persons who are spreading infection, will make the medical officer of health more aware than hitherto of the numbers of infections occurring in his area.

SYPHILIS

Survival of *Spirochaeta pallida* in frozen plasma

M. M. Ravitch and J. W. Chambers (1942) found that blood plasma, which had been heavily infected experimentally with *S. pallida* and stored at 20° C., could infect rabbits at the end of twenty-four hours but could not do so at forty-eight hours or later. This accords with the findings of T. B. Turner and T. H. Discker (1941), but not with those of O. Bloch, Jun. (1941), who infected rabbits with blood contaminated by *S. pallida* which had been stored for seventy-two hours, but not with blood stored for longer than this period.

Serum diagnosis

False positive reactions.—The subject of false positive reactions to serum tests for syphilis was discussed in Medical Progress (Critical Survey section) 1943, p. 87, but in view of its importance and of the fact that the conditions responsible for such non-specific reactions are not yet completely understood, no excuse is necessary for reverting to it. The practitioner who is not a bacteriologist is apt to leave the mysteries of the syphilitic serum tests to the laboratory worker, and to be content to accept the report of the latter almost as a verdict on the question of syphilis in his patient. Such a passive attitude may not have been fraught with great danger when blood tests

were ordered chiefly on suspicion of syphilis, because in such cases if the report is positive it is usually accepted as confirmation of the suspicion, and treatment of the patient is started.

In recent years, however, the practice of testing the blood of large groups of people—pregnant women, blood donors, candidates for marriage and so forth—as a matter of routine precaution has grown rapidly and will inevitably increase as the general public become more and more syphilis-conscious and learn of the tendency of the disease to remain latent for many years together. Consequently it has become very important that practitioners should be well acquainted with the limitations of blood tests for syphilis, lest on the one hand they diagnose syphilis unjustifiably or on the other blame the laboratory worker for false positives which are not attributable to technical errors but to peculiarities of certain sera. A clear understanding of the conditions liable to cause false positive reactions and of the steps to be taken when the laboratory report conflicts with the clinical data should help to reduce the number of domestic tragedies which are inevitable as the custom of routine testing for syphilis grows. The mention of tragedies is not intended to be interpreted as condemnation of routine testing—the gain from this is likely to be far greater than the loss—but only as a warning against misuse of a very valuable antisyphilitic weapon.

In *Medical Progress* (Critical Survey section) 1943, pp. 88 and 89, a number of conditions were mentioned which are liable to cause false positive reactions; they are additional to those mentioned in the *Encyclopaedia* (Vol. XI, p. 542). A useful understanding of such conditions is afforded by study of a recent article by H. Sachs (1942). He considers that in blood tests for syphilis the theoretical ideal of sensitivity capable of detecting the least possible trace of syphilis reagent combined with complete specificity will never be reached because of the presence in all tissue extracts of the 'ballast material' to which the relatively minute amount of specific antigen is attached and which may in certain circumstances react with the serum under test in the same way as does the specific antigenic fraction with syphilis reagent; this is especially apt to occur when the globulins in the serum are labile. Such 'lability reactions' are apt to occur in conditions that increase the blood sedimentation rate.

As pointed out by Sachs in the early days of the Sachs-Georgi test and as exploited in the Kahn verification test, such non-specific reactions may be prevented to a large extent by preliminary heating of the serum to stabilize the globulins and by conduct of the test at higher than room temperatures. An alternative, employed in the Meinicke test, is the use of salt solution of higher than physiological concentration. It appears probable from all this that serum tests in which unheated serum is used without the precaution being taken of mixing it with saline more concentrated than physiological saline, or in which the reaction is read after the mixture has been kept no warmer than at room temperature, or when both such conditions exist, must be always liable to give false positives in certain circumstances; for purposes of final diagnosis they should be displaced by those in which the test is conducted at 37° C. or higher temperatures.

B. E. Diamond (1942) found that some batches of antigen for the Kolmer method of the Wassermann test were more liable to give non-specific fixation than were others tested, this is in spite of the elaborate preparation of Kolmer antigen designed to remove fractions favouring non-specific reactivity. M. N. Green and G. F. Forster (1942) have pointed out that the Kahn verification test, besides being useful for the elimination of non-specific reactions, is valuable for the discovery of syphilis because conduct of the test at 37° C. or, apparently better, at 45° C. evoked positive syphilitic reactions which were not apparent when the test was carried out at room temperature or at 0° C.

G. H. Hodel (1942) has laid down a useful series of steps adopted by the Los Angeles County Health Department to settle the question of syphilis when positive serum reactions are not supported by the history or clinical signs. They are (1) inquiry into the history, which should not only search for evidence of syphilis but should rule out conditions likely to cause false positive reactions; (2) complete physical examination; (3) further blood tests repeated at least three times by complement-fixation and by flocculation; (4) X-ray examination of the heart and aorta; (5) test of the spinal fluid; (6) examination of contacts; and (7) evaluation of all the evidence elicited by the above procedures. Perhaps not all the above steps may be always necessary to enable the practitioner to arrive at a conclusion, but before a diagnosis of syphilis is made,

positive evidence supporting the blood reaction should have been obtained. Response to further blood tests may serve to justify exclusion of syphilis or at least postponement of the decision concerning presence of syphilis in the patient and of antisyphilitic treatment, as in the following case, recently seen by me, which may serve as an example of the difficulties sometimes encountered.

A virgin aged fifty volunteered as a blood donor but her blood was found to give a positive Wassermann reaction. This reaction was repeated in two laboratories with two further specimens; at the same time the Kahn reaction varied between positive and doubtful. Her private practitioner sent her to me for advice on treatment. Like him, I failed to find any clinical evidence or history suggestive of syphilis and took a further specimen of blood which was divided into two portions. The first of these was tested in one laboratory by routine Wassermann and Kahn methods, with negative results. In this laboratory the heart used for Wassermann extract is always quite fresh, and may therefore be less liable to give non-specific reactions with certain sera than is extract made from older hearts. The second portion was tested by G. M. Richardson in the Ministry of Health's laboratory for syphilitic serum tests with the following interesting results: by the routine Wassermann (Harrison-Wyler) method using human heart antigen the specimen gave a strongly positive reaction, and the same occurred with the Richardson modification of the Harrison-Wyler method. Using an ox-heart antigen the routine method gave a single plus reaction but the Richardson modification, which usually strengthens specific reactions and weakens non-specific ones, gave an almost negative reaction. By the Kahn test conducted at room temperature and at 0° C. the reaction was doubtful, but at 37° C., which strengthens specific reactions and weakens non-specific ones, it was negative. Treatment was withheld and advice given to have the blood tested on similar lines at monthly intervals for some time. The outcome confirmed the opinion that the patient was not suffering from syphilis.

The case illustrates the fact that occasionally a blood specimen may give a false positive reaction when tested by a method which has an almost irreproachable reputation so far as such reactions are concerned, and that the matter may be cleared up only by further testing with other antigens and by a flocculation method conducted at 37° C.

The value of the quantitative method in serum tests.—Recent papers expounding the value of titrating the strength of a serum reaction for syphilis provoke the comment that the method is not new, although recent developments in the treatment of syphilis may have widened the scope of its usefulness. A. Vernes in many publications, including his *Atlas de Syphilimétrie* published in 1920, has always maintained that in every case the strength of the reaction should be measured at regular intervals and charted; the fluctuations or otherwise of the titre are then used for guidance in diagnosis, in treatment, and in tests of cure. In 1921 G. Dreyer and H. K. Ward published details of their 'sigma' modification of the Sachs-Georgi test, one great merit of which is its automatic declaration of the strength of the reaction. The value of this method in the management of late cases of syphilis was pointed out in the *Encyclopaedia* (Vol. XI, p. 620), where it was stated that the decreasing titre of the reaction under treatment showed the effect of this when the ordinary diagnostic test might show no change for course after course of treatment.

A disadvantage of these methods is that they are not so sensitive as could be desired, and that recommended by R. L. Kahn (1925) is probably better. In the Kahn quantitative test the more sensitive antigen of his presumptive test is employed, and the strength of the reaction is four times the maximum dilution of the serum which causes definite flocculation. The method does not seem to have attracted great attention until in 1939 R. L. Kahn expounded its advantages at some length; they included measurement of the effect of treatment, the diagnostic indication of a temporary rise in the titre following a provocative injection of an antisyphilitic remedy, and the warning of a coming relapse conveyed by a rise in the titre. A further fillip to its popularity has come from the more recent introduction of shorter, more intensive forms of treatment, since in these the authors wish to know as accurately as possible how the syphilitic process is faring behind the veil of clinical latency. Here, to wait until a diagnostic test has shown a change in the reaction is to remain in the dark far longer than is desirable. On the one hand, after what eventually proves to have been a sufficient treatment the diagnostic test may not show any reversal for many weeks, during which a quantitative test would have shown a steady fall in the titre; on the other hand, when the reaction has become negative following inadequate treatment the diagnostic test may not show any change in the direction of positivity when a

quantitative test would give early warning through a steadily rising titre.

The following short examples of the value of the quantitative Kahn test may be quoted. W. M. Simpson, D. L. Rose and H. W. Kendell (1942) obtained early warning from a rise in the titre of the reaction during the course of artificial fever treatment of early syphilis that fever alone was insufficient for the cure; the institution of chemotherapy in these cases at once set the titre on a downward course. In a later paper D. L. Rose, W. M. Simpson and H. W. Kendell (1942) reported on the effect in twenty-three cases of early syphilis, of a ten-hour session of artificial fever during which mapharsen (arsenoxide) was administered either by drip-feed (two cases) or by multiple injections, the total dose ranging from 120 to 240 milligrams. The serum was tested quantitatively each week thereafter for a minimum of six months, and the duration of positivity appears to have depended entirely on the original titre, ranging from twenty-one days in a case with an initial titre of four units to 176 days in one with an initial titre of 3,160 units. A simple diagnostic test would have made it appear that the effect of the treatment on the syphilitic process in the quickly reversed cases had been greater than in those which remained positive for some months, whereas the courses of their titres appear to have shown that in both it was only a matter of getting rid of reagin after stoppage of the antigenic action of the spirochaete. By the same method H. W. Kendell, D. L. Rose and W. M. Simpson (1942) obtained the hint that a prolonged course of fever and chemotherapy might not achieve any more than a single day's treatment on the same lines.

A complicating factor in the use of a quantitative method with a very sensitive antigen might be the intervention of a biological change in the patient, causing non-specific reactions of the type termed by Kahn 'general biologic' (See Medical Progress (Critical Survey section) 1943, p. 88), and by Sachs (see above) 'lability', since these would be more apparent with such an antigen as is used for the Kahn presumptive test than with that used for the Kahn standard. It seems possible that such a complication would be avoided by conducting the test at a temperature of from 37° C. to 45° C., as might be inferred from what was said in the earlier part of this Survey.

Treatment

Massive arsenotherapy.—A one-day cure with a single session of artificial fever in conjunction with chemotherapy reported by Rose, Simpson and Kendell has been mentioned above.

A great advantage claimed for massive arsenotherapy is that it reduces considerably the chances of failure through premature discontinuance of treatment on the patient's part. For this reason it should be particularly applicable to infants and children with congenital syphilis, since parents and guardians of such patients are very prone to neglect their duties in respect of ensuring continuance of the patients' treatment. I. M. Levin, S. J. Hoffman, D. S. Koransky, I. B. Richter and B. Gumbiner (1942) do not seem, however, to have been very successful in thirty-two cases of congenital syphilis in infants and children treated by this means, although they stepped up the total dose of mapharsen to 15 milligrams per pound of body weight (given in five days) or approximately twice as much per pound as is usually given to adults in the same time. In infants they fastened a cannula in an internal malleolar vein and administered the remedy by drip-feed during ten hours of each day, closing the cannula with an obturator on suspension of the administration each evening. The serum reactions appear to have been reversed by the treatment in only twelve of the thirty-two cases. In contrast to this experience, in four cases of acquired syphilis in children there appears to have been no failure; the suggestion is that congenital syphilis is more resistant to treatment than is acquired syphilis.

Ruth A. Boak, C. M. Carpenter, N. Jones, R. H. Kampmeier, W. S. McCann, S. L. Warren and J. R. Williams, Jun. (1942) have shown conclusively that, although a single session of artificial fever lasting from nine to fifteen hours at 41° to 41·5° C. may cause *S. pallida* to disappear promptly from syphilitic lesions and the latter to heal up just as well as under two weeks' chemotherapy, it does not cure syphilis; they attribute the failure to nests of spirochaetes in parts such as the mucous membrane of the mouth where the temperature was not as high as that of the body generally. The failure of artificial fever alone to effect a cure in their cases accords with the experience of Rose, Simpson and Kendell mentioned above.

Concurrent versus alternating arsenical and heavy metal treatment.—In the United

States of America the method of administering arsphenamine compounds in courses alternating with courses of heavy metal is generally preferred to that, most prevalent in Great Britain, of giving the two types of remedy concurrently. D. Kahn and S. W. Becker (1942) in reporting good effects of the concurrent method quote N. M. Clausen, B. J. Longley and A. L. Tatum (1942) whose results in experimental syphilis caused them to say that 'the therapeutic coactions of bismuth and arsenical compounds are completely additive, while their co-toxicities are less than additive'. Like these authors, Kahn and Becker think that the concurrent method affords the same results when smaller doses of each type of remedy are given than when each remedy is given alone. The finding that in animals smaller doses of arsenical compounds achieve more when the two remedies are given concurrently is not new. F. Lehnhoff-Wyld (1924) found in experimental trypanosomiasis that the curative dose of sulpharsphenamine was smaller when another metal was in the animal's circulation at the time the arsenical remedy was administered. He used a number of metals, and the best results appear to have followed the concurrent administration of zinc.

CHANCROID

Prevention and treatment with sulphonamide remedies

The methods commonly employed for the prophylaxis of venereal diseases, principally washing with soap and water and the application of mercurial disinfectants, have generally seemed to be disappointing so far as chancroid is concerned, and the recent experimental work of R. B. Greenblatt, E. S. Sanderson, F. Mortara and H. S. Kupperman (1943) seems likely to prove a valuable advance in prophylactic technique. They found in experimental inoculations of nineteen volunteers with virulent cultures of *Haemophilus ducreyi* that soap solutions and various mercurial preparations respectively when applied to the inoculated areas an hour later generally failed to prevent the development of typical chancroids. On the other hand, application of various sulphonamide powders succeeded in five out of seven cases. Application of sulphonamide ointments in a water-soluble base succeeded in twelve out of twenty-seven cases, and 25 per cent sulphanilamide or 25 per cent sulphadiazine in an ointment with 25 per cent calomel (introduced for its antisiphilic effect) prevented infection in eleven out of thirteen inoculations. Ingestion of sulphathiazole generally succeeded. Thus in four females forty inoculations were made; two patients took respectively 2.5 and 5.0 grammes of sulphathiazole for two days immediately after the inoculation, one had 6 grammes a day for seven days immediately before, and one had 3.5 grammes on the day before and 5 grammes a day for two days immediately after the inoculations. Chancroid developed in only one of the forty areas.

In all but one of the cases in which the inoculated area was left untreated, chancroids developed; they responded well to oral administration of sulphonamides, healing in from five to seven days; the application of sulphonamide powders to the lesions was slower in effect. Other experiences in prophylaxis of chancroid by sulphonamides are mentioned below.

GONORRHOEA

Cultural diagnosis

In view of the fact that in circumstances favourable to culture of the gonococcus this method of diagnosis is superior to that by microscopic examination of stained smears and should be employed whenever practicable, methods of reducing the mortality of the gonococci in the specimen during the period of transportation to the laboratory are particularly important. A. Cohn (1942) found that some strains of gonococci seem unable to stand even a short delay between removal from the body and incubation on a favourable medium. A good transporting medium was made of 2 per cent Difco proteose peptone No. 3, 0.75 per cent agar, and 0.2 per cent cystine hydrochloride. Overgrowth with secondary organisms was best prevented by keeping the specimen cold, and in this connexion the finding by E. S. Sanderson and G. G. Allison (1942), that packing the specimen in dry ice is very successful, seems important. Their specimens were collected on wool swabs which had been soaked in 15 per cent glycerin in a buffered solution of pH 7.4. The swabs on sticks were placed in tubes which were packed in dry ice. Lucy S. Heathman and Margaret Higginbotham (1942) found that enrichment of the transporting medium with cystine was an advantage. S. D. Allison, Ruth Charles and C. M. Carpenter (1942) found that gonococci remained alive in urine long enough to make this a practicable medium for the transport of the specimen

to the laboratory. In samples from 127 male patients eighty-six provided cultures of gonococci one to three hours after removal, seventy-two at twelve to fifteen hours, fifty-three at eighteen hours, thirty-five at twenty-six hours, eighteen at thirty-six hours, and two at forty-eight hours; it was found in the older specimens that it was advantageous to plant from the centrifuged deposit of the urine.

Prophylaxis by sulphonamides

M. Joses (1942) found in the Philippines in 350 naval ratings who had not undergone any prophylactic disinfection that administration of sulphathiazole was very successful in preventing gonorrhoea and chancroid. This experience was substantially confirmed by E. F. Kline and T. C. Ryan (1942) in the case of 1,000 ratings; they gave 2 grammes on the morning following the exposure and 2 grammes five hours later. J. A. Loveless and W. Denton (1943), dealing with a body of 1,400 negro troops, adopted the practice of giving each 2 grammes of sulphathiazole on leaving the fort, 2 grammes on return, and 2 grammes the following morning. The result in the men who took this prophylactic course completely was an incidence of 8 gonorrhoea and 6 chancroid cases per 1,000 per annum as compared with 171 and 52 respectively in a control group of about 4,000 soldiers in the same camp.

Possible ill effects from routine use of sulphonamides in prophylaxis.—The question of the advisability of using sulphonamides so indiscriminately as in the cases just mentioned has been investigated by F. W. Reynolds, Mildred S. Evans and F. B. Walsh (1943) from the point of view of its effect on ocular function. They found in sixteen volunteers, half of whom took 4 grammes of sulphathiazole and half the same dose of sulphadiazine in twenty-four hours, that in an important proportion there was a transitory interference with adduction and abduction, power of fusion and convergence and depth of perception; there was also in some enlargement of the blind spot for colour. The effect had generally disappeared thirty-two hours after the last dose, but the authors thought their results supported the warnings which have been given against the indiscriminate use of these compounds, and especially so in persons who require a maximum efficiency of ocular function.

Treatment

W. Greuer (1942), in fifty cases of gonorrhoea in women treated by the Miescher plan of giving 1 gramme five times on each of two days, had only 74 per cent of successful results, but H. Lohe and R. Brett (1942) had 85·5 per cent of success with one such course in 1,100 women and 97·5 per cent with two courses. They tried prolonging the treatment for three days, and in 140 cases claimed 95·8 per cent of successes. In 300 male cases their successes with the two-day treatment were 89·4 per cent with one course and 95·4 per cent with two courses. On the important question of the interval between the end of treatment and appearance of a relapse they found in the female cases that their 14·5 per cent of relapses from one course were made up of 10·6 occurring before the tenth day and 3·9 after this. In an analysis of forty-six cases of late relapse they showed that twenty occurred from the eleventh to the thirteenth day, twenty-one from the fourteenth to the twentieth day, and one each on the twenty-third, twenty-fifth, twenty-sixth, thirty-fifth and fifty-sixth days. Most of the relapses were acute and obvious so that the problem of tests of cure after sulphathiazole treatment seems to be relatively simple. Other observations by these authors suggest that if the patient is pregnant when the treatment is given it is advisable to test for cure again after the parturition.

F. J. G. Jefferiss and G. L. M. McElligott (1943) in male Forces cases had 89·5 per cent of cures with a two-day treatment with sulphathiazole and 90 per cent with one prolonged to three days. Although they carried out provocative tests of cure as ordained by conscientious workers, they confessed that they had not seen any advantage in them. J. P. Pappas (1942) claimed twenty-three successes in twenty-eight soldiers treated each with a single dose of sulphathiazole, that recommended being 5 grammes.

Causes of failure of sulphonamide treatment of gonorrhoea.—J. Petro (1943) classifies causes of failure of sulphonamide treatment under the headings of (1) low blood concentration of the drug, which does not seem to have applied in his cases; (2) obstruction of free transport of the drug to all foci of infection; (3) obstruction to efficient drainage of foci and (4) infection with sulphonamide-resistant strains of gonococci. He gives evidence of a relation between resistance *in vivo* and resistance *in vitro* and records valuable examples of this in a male patient and in the woman from

whom he contracted the infection. He quotes in support of his work the findings of K. Schmith and F. E. Reymann (1940) who showed that there is a wide difference between the resistance of different strains of the gonococcus *in vitro* and a close relationship between this and response to treatment. Although it has been shown that the resistance of a strain of the gonococcus can be increased by its exposure to sublethal concentrations of sulphonamides, Schmith and Reymann showed that not all such resistance is due to this cause, as they found wide differences in the resistance of fifty laboratory strains of gonococci which had been isolated in the pre-sulphonamide era.

It seems legitimate to conclude from all the work on resistance that in the treatment of gonorrhoea with sulphonamide remedies the dosage at the outset should be large because (1) the infecting organism may be relatively resistant or (2) in a relatively inaccessible focus, and if for either or both these reasons the remedy reaches the organism in a sublethal concentration, it may make it still more resistant. The transmission of such strains to other persons may eventually increase the general difficulty of treating gonorrhoea.

Treatment of sulphonamide-resistant gonorrhoea with penicillin.—For the treatment of sulphonamide resistance in gonorrhoea chief reliance has hitherto been placed on combining artificial pyrexia with the sulphonamide treatment, but perhaps the use of penicillin will prove to be a better way. W. E. Herrell, E. N. Cook and L. Thompson (1943) report that they have successfully treated with penicillin three patients who had proved completely resistant to sulphonamide treatment administered in various forms. The penicillin was administered by drip-feed intravenously during two and a half to three and a half days, and the result in each case was a dramatic disappearance of all symptoms in relatively a few hours. Further experience (unpublished at the time of writing) has amply borne out the promise of these earlier trials.

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RECENT DEVELOPMENTS IN DRUG THERAPY

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OFFICIALLY APPROVED NAMES OF DRUGS

In previous articles prominence has been given to the endeavours of the General Medical Council and the Pharmaceutical Society of Great Britain to establish approved or official names for drugs which have been found to be of therapeutic value. The objectives are to promote the use by medical practitioners, when prescribing any particular drug, of a non-proprietary name available to all manufacturers and to discourage manufacturers from evolving multiple proprietary or brand names for the same substance. The medical practitioner should realize that if he prescribes a remedy under a proprietary name the pharmacist is bound by law to dispense only that special manufacturer's preparation (which he may not possess and may have difficulty in obtaining) although he may stock several equivalents. Delay in treatment often results because the pharmacist cannot dispense an equivalent to a proprietary or brand preparation unless he first obtains the prescriber's consent. If, as is advised, medical practitioners order drugs under their officially approved names, the pharmacist may supply either a non-proprietary or a proprietary product which conforms with the official standards laid down for the particular remedy which has been prescribed. If the medical practitioner has special reasons for requiring the product of a particular manufacturer, he may ensure that this is supplied by putting in abbreviated form the name of the required manufacturer after the approved name. It is pointed out that the recognition of an approved name by the British Pharmacopoeia Commission does not necessarily imply that the drug will be introduced into the Pharmacopoeia.

The Pharmacopoeia Commission invites the cooperation of manufacturers in the choice of approved names for new drugs and deprecates the introduction of other names for substances to which approved names have been given. The following are the guiding principles in the selection of approved names.

(1) Names of chemicals should preferably be free from any anatomical, physiological or therapeutic suggestion, this may not always be achieved in the case of biological products.

(2) The accurate chemical name should be used if suitable, but if unsuitable a name should be formed by a combination of its significant syllables with an indication of the potent element or constituent of a compound.

(3) Names should be at most of four syllables.

(4) Names should be distinctive in sound and spelling and should not be liable to be confused with names already in use.

(5) Names difficult to pronounce or to remember should be avoided.

(6) Terminal capital letters or numbers should be avoided.

(7) Names used in or adopted for the United States Pharmacopoeia should be used either as principal titles or as synonyms.

(8) Names used in the *British Pharmaceutical Codex* or in *New and Non-Official Remedies* should be preferred.

(9) The following recognized terminations should be used.

-ine (Latin -ina) for alkaloids and organic bases

-in (Latin -inum) for glycosides and neutral principles

-ol for alcohols and phenols (-OH group)

-al for aldehydes

-one for ketones and other substances containing the CO group

-barbitone or -itone for drugs of the barbiturate group

-caine or -aine for local anaesthetics.

Official recognition has now been given to the names of the following drugs which were described in Medical Progress (Critical Survey section) 1943, p. 94: diphenan, (butolan), dithranol (cignolin), ethisterone (ethinyltestosterone, lutocyclin, lutogyl, pregnenolone, progestoral, proluton C), menaphthone (menadione U.S.P. XII, 2-methyl-1:4-naphthoquinone), mesulphen (mitgal), soluble phenytoin (epanutin,

eptoin, sodium diphenylhydantoinate, solantoin, soluble dilantin) and sulphacetamide (albacid).

Names recently approved

Amethocaine hydrochloride.—This is *p*-butylaminobenzoyldimethylaminoethanol hydrochloride (decicain, pantocaine, anethaine). In 2 per cent solution this is a useful surface anaesthetic for mucous membranes. It does not constrict blood vessels and is therefore usually combined with 0.005 per cent of adrenaline. When injected as a local anaesthetic it is about ten times more effective than procaine, but only five times more toxic. Hence it has a slightly higher safety margin and further its effect is usually prolonged to two or three hours. Solutions of 0.1 per cent are suitable for local injection or nerve-blocking, 0.025 to 0.05 per cent for infiltration anaesthesia; for intraspinal anaesthesia, 0.01 to 0.02 gramme ($\frac{1}{8}$ to $\frac{1}{4}$ grain) is dissolved in 2 to 4 cubic centimetres of the patient's cerebrospinal fluid.

Cyclobarbitone.—*Cyclo*-Hexenylethylbarbituric acid (phanodorm, phanodorn). This is a hypnotic more rapidly excreted and therefore of less lasting action than barbitone. Dose in tablets: from 0.2 to 0.4 gramme (3 to 6 grains).

Dienoestrol.—*Di*-*p*-hydroxyphenylhexadiene. Dienoestrol has the same action as the ovarian follicular hormone oestrone and can be given orally. Its dose is one-tenth that of stilboestrol but it is somewhat less effective. Dose: from 0.0001 to 0.0005 gramme (see Medical Progress (Critical Survey section) 1943, p. 98).

Diodone.—A combination of 3:5-diiodo-4-pyridone-*N*-acetic acid and diethanolamine (perabrodil, pyelosil). Diodone contains about 50 per cent of iodine. A 35 per cent solution in dosage of 20 cubic centimetres at body temperature is used by slow intravenous injection to give radiographic opacity to blood vessels and to the biliary and urinary tracts during its excretion.

Hexazole.—*Cyclo*-Hexylethyltriazol (azoman, triazole). Hexazole is used as a 5 per cent solution in doses increasing from 1 to 2 cubic centimetres (15 to 30 minims) intravenously, or in twice these amounts intramuscularly, in the convulsive treatment of schizophrenia. Treatment by hexazole is considered to be less unpleasant for the patient than by leptazol but the risks of both are such that this form of therapy should be used in mental hospitals only (W. Mayer-Gross and A. Walk, 1938; D. E. Sands, 1939).

Meprochol.—Trimethylmethoxypropanylammonium bromide (esmodil). Meprochol is a stimulant of the parasympathetic nerve endings. It is advised as a 0.3 per cent solution, used hypodermically or intramuscularly, in doses of 0.5 to 1 cubic centimetre (7 to 15 minims) in the treatment of post-operative intestinal atony and paralytic ileus; more extensive clinical use will determine its relative value.

Pethidine hydrochloride.—The carboxylic acid ethyl ester of 2-methyl-4-phenylpiperidine (dolantin, dolantal). Dose: orally as tablets, 0.025 to 0.05 gramme ($\frac{1}{8}$ to $\frac{1}{4}$ grain); by intramuscular, or very slowly in urgent cases by intravenous, injection, 0.05 to 0.1 gramme ($\frac{1}{4}$ to $1\frac{1}{2}$ grain) dissolved in 2 cubic centimetres. Pethidine hydrochloride is an analgesic and also relaxes spasm of plain muscles such as those of the intestine, bile-duct, ureters, uterus and arteries. It has been used with success to relieve pain and spasmodic contraction in severe intestinal colic during the passage of renal and biliary calculi and to relax the arterioles. As an analgesic it has proved useful in neuritis, arthritis and carcinoma (R. V. Christie, 1943; G. FitzGerald and B. McArdle, 1943).

Pheniodol.— β -(4-hydroxy-3:5-diiodophenyl)-*o*-phenylpropionic acid (biliselectan). Pheniodol is a useful contrast medium for radiography of the gall-bladder and when administered orally gives shadows as satisfactory as those which result from an intravenous dose of tetraiodophenolphthalein. Dose: orally, 3 grammes (45 grains) (M. Dohrn and P. Diedrich, 1940, 1942).

Pholedrine.— β -(4-hydroxyphenyl)-isopropylmethylamine (veritol). Dose: orally, 0.025 to 0.05 gramme ($\frac{1}{8}$ to $\frac{1}{4}$ grain) in tablets; intramuscularly or intravenously, 0.25 to 1 cubic centimetre of a 2 per cent solution. Pholedrine acts like adrenaline and is used to raise blood pressure in the prevention and treatment of surgical shock. Its action is less rapid but more prolonged than that of adrenaline, the maximum rise occurring in twenty minutes and lasting about one hour (P. C. Elmes and A. A. Jefferson, 1942; H. Dodd, 1942; E. Landau, V. Logue and H. Kopelman, 1942).

Recently methedrine or *N*-methylamphetamine has been recommended as superior to pholedrine. It may be given subcutaneously, intramuscularly or intravenously.

Intravenous injections raise blood pressure immediately, while intramuscular injections act in two to ten minutes. Dose: intramuscularly, 0.015 to 0.03 gramme ($\frac{1}{6}$ to $\frac{1}{2}$ grain); intravenously, 0.01 to 0.02 gramme ($\frac{1}{6}$ to $\frac{1}{2}$ grain). Both methods of administration have been used simultaneously in cases of severe shock. The average rise of systolic pressure was from 66 millimetres to 138 millimetres and of diastolic pressure from 52 millimetres to 84 millimetres. The pressor effect is regarded as superior to that of adrenaline, ephedrine and pholedrine because the blood pressure is restored to its pre-operative level, or to within 90 per cent of it, for several hours and one injection is therefore usually sufficient (H. Dodd and F. Prescott, 1943).

THE SULPHONAMIDES

Mode of action

It was pointed out in 1943 that the action of the sulphonamides as inhibitors of bacterial growth depends upon the bacteria being prevented from utilizing the *d*-aminobenzoic acid which is essential for their growth; their inhibitory power in fact depends upon the relative concentration of the growth factor and of the inhibitors in the culture medium or tissues. It appears that *p*-aminobenzoic acid forms the natural substrate for an enzyme or complex enzyme system which is antagonized by the sulphonamides. The relative effective concentration varies for different bacteria and the term, anti-bacterial index, has been used to express the ratio between the antagonizing concentration of the inhibitor and that of the growth factor. Thus with *Streptococcus pyogenes* the index for sulphanilamide is 25,000, that is to say 25,000 times as much sulphanilamide as *p*-aminobenzoic acid is necessary in the medium or tissues to obtain the inhibitory action.

The principle has also been established that the substitution for the acid or carboxyl group, $-\text{COOH}$, in a growth factor by the sulphone, $-\text{SO}_2\text{OH}$, or sulphamino, $-\text{SO}_2\text{NH}_2$, group, produces compounds which will inhibit the growth of bacteria requiring that particular growth factor.

Another essential growth factor for certain bacteria, for example *Strep. pyogenes* and *pneumococcus*, is pantothenic acid, its inhibitory agent is pantooyltaurine. The anti-bacterial index of pantooyltaurine for streptococci is 500 and for pneumococci 1,000; hence it is much more potent as an inhibitor of bacteria requiring pantothenic acid than is sulphanilamide for those requiring *p*-aminobenzoic acid. Therapeutic trials with pantooyltaurine have not yet been reported (H. McIlwain, 1942; W. B. Wood, Jun., 1942; Wood and R. Austrian, 1942; H. I. Kohn and J. S. Harris, 1941).

Sulphonamide drugs and war wounds

The principles for the use of sulphonamides in war wounds have been well represented by L. E. H. Whitby. (1) The drug to which the infecting organism is particularly sensitive should be used. Sulphanilamide should be chosen for prophylaxis by oral administration, local application or both. With an established infection either sulphapyridine or sulphathiazole is indicated orally. Polyvalent gas gangrene antitoxin should also be given, since these drugs have not any action on *Clostridium oedematiens*. (2) An effective general, intraspinal or local concentration must be maintained by four-hourly oral dosage night and day. For wound applications the less soluble sulphapyridine is not so satisfactory as sulphanilamide and sulphathiazole; a mixture (2 : 1) of the last two is recommended. Sulphathiazole is essential if gas gangrene (*Vibrio septique* or *Cl. Welchii*) infection is suspected. (3) The drugs act best on small numbers of bacteria, therefore the wound should be clean and free from pus, dirt and foreign bodies, all of which retard or inhibit the action and shelter bacteria. (4) If adequate dosage at four-hourly intervals fails to produce an effect in from seven to ten days, it is evidence that the organism is insensitive and treatment should be discontinued. If symptoms abate, the drug should be continued for forty-eight hours after the desired clinical effect has been brought about, lest relapse occur (L. E. H. Whitby, 1942).

Investigations on experimentally infected wounds have shown that the soluble and easily absorbed sulphanilamide acts as a bacteriostatic agent for a short time only, but its action is more prolonged if it is in an oily base or (although to a less extent) in an oil and water emulsion. A suitable preparation is sulphanilamide 10 to 30, cotton-seed oil 30, triethanolamine 1, stearic acid 2, cetyl alcohol 1 to 4, and water to 100.

The most satisfactory preventive of streptococcal infections was found to be sulphathiazole in micro-crystals suspended in saline, but more easily available is a 30 per

cent suspension of sulphanilamide in an oil and water paste, the strength for use in large wounds being reduced to 10 or 15 per cent, so that not more than 15 grammes of sulphanilamide is used (F. Hawking, 1942).

Experiments on the rate of absorption of sulphonamides from various aqueous and oily media applied to surface wounds in rabbits showed that sulphanilamide was rapidly absorbed from a glycerin-gelatin preparation (sulphanilamide 15, gelatin 35, glycerin 10, chlorocresol 0.2, phenylmercuric acetate 0.001, water to 100) and also from gauze impregnated with sulphanilamide. *In vitro* tests showed that diffusion of sulphanilamide was delayed by incorporating it in an oily base or in a water in oil emulsion, and delay in absorption can also be achieved by using an aqueous suspension of a less soluble form such as sulphathiazole. The following is recommended for surface application or for impregnating gauze. Sulphanilamide or sulphathiazole 10, chlorocresol 0.2, stearic acid 3.5, yellow beeswax 1.5, wool fat 1.5, cotton-seed oil 27.0, solution of sodium hydroxide (20 per cent) 2.1, distilled water 54.2 (A. T. Fuller, F. Hawking and M. W. Partridge, 1942).

In Germany it has been recommended that wounds in which infection is suspected should be treated with a 1 in 10 mixture of marfanil and sulphanilamide—marfanil is 4-aminomethylbenzenesulphonamide. If there be a risk of general infection 3 to 6 grammes (45 to 90 grains) of marfanil-sulphanilamide is given daily for a week (Haferland, 1941).

Initial dressings with sterilized sulphanilamide powder contained in a Cellophane envelope, or a field dressing impregnated with sulphanilamide or with a semifluid suspension of it from a collapsible tube, are advocated when surgical treatment cannot be given quickly (Hawking).

The occurrence of a fatality from tetanus infection has led to the recommendation that sulphanilamide powder should be sterilized and issued in sterile packets containing 5 grammes. Small-scale sterilization methods recommended were (1) dry heat maintained at 150° C. for one hour by means of a paraffin bath (H. Berry, 1942), (2) dry heat maintained at 150° C. for one hour in an electric oven and (3) autoclaving at 15 lb. pressure for thirty minutes with special precautions (W. J. Buckland, 1942).

The clinical value of sulphathiazole powder in the local treatment of grossly infected wounds after they have been swabbed clean with normal saline, has been emphasized, but with the reservation that there is a tendency to capillary haemorrhage from the margins of the wound and to excessive granulation. The cleansed wound after being dried with gauze was sprinkled with a layer one-eighth of an inch thick of sulphathiazole and covered with gauze and Gamgee tissue; applications were renewed every two or three days. From initial trials it was considered that warm (110° F.) saturated solutions of sulphonamides allowed to drip for from one and one-half to two hours upon an open wound may prove advantageous because bacteria exposed to sulphonamides are more susceptible to heat (H. N. Green and T. Parkin, 1942).

Reaction and resistance to sulphonamides

A study of sulphonamide resistance in a large number of cases of male gonorrhoea indicates that resistance may be (1) acquired, as a result of initial inadequate dosage, (2) relative, in which even adequate dosage has to be supplemented by a second or third course before cure can be achieved and (3) absolute, in which gonococci persist despite adequate and sustained sulphonamide treatment. Amongst possible causes of relative and absolute resistance are a low blood concentration of sulphonamide due to slow absorption or rapid excretion; imperfect access of the drug to the infected tissue; impaired natural defences; and infection with resistant gonococcal strains which may be initiated by inadequate dosage of an earlier host and can apparently be transmitted to a new host. Alternatively, some strains may become resistant or 'drug fast' to sulphonamide by elaborating themselves the necessary growth factor or an intermediate factor which acts as a substrate in their enzyme complex (J. Petro, 1943).

Insufflations twice daily with sulphanilamide powder have been curative, usually within a week, in diphtheria carriers having a double nasal infection with *Corynebacterium diphtheriae* and haemolytic streptococci (Joan M. Boissard and R. M. Fry, 1942). Sulphathiazole powder has also been advocated for this purpose (J. Goldman and W. H. Patterson, 1942). Sulphanilamide has been reported as effecting recovery of acute disseminated lupus erythematosus with lymphadenopathy after several other agencies had failed, but as anti-serum, pentnucleotide and transfusion were also given it is difficult to assess the value of the sulphanilamide (J. E. G. Pearson, 1943).

Attention has been drawn to the more frequent occurrence of sunlight eruptions in the Tropics after sulphanilamide than after sulphapyridine therapy. The eruptions arise about the eighth to tenth day of administration and are usually erythematous papules. Less common are vesication, pustulation and desquamation (R. G. Park and W. M. Platts, 1942).

Sulphathiazole

A 10 to 20 per cent suspension of micro-crystalline sulphathiazole in neutral saline forms a white cream which is recommended as a wound dressing because the fine crystals, having a larger surface area, are more rapidly absorbed. Sulphathiazole is to be preferred because it is more actively bacteriostatic and has a wider range of organismal inhibition than sulphanilamide whilst it is also more soluble than sulphapyridine and sulphadiazine (L. A. Chambers, T. N. Harris, F. Schumann and L. K. Ferguson, 1942).

Sulphathiazole is considered to be more efficacious than sulphapyridine in the treatment of compound fractures infected with *Staphylococcus pyogenes*. The treatment should be both pre-operative and post-operative and should also be a combination of local and oral administration (J. F. Heggic, A. W. Kendall and R. M. Heggic, 1942).

Sulphathiazole should not be applied as a bacteriostatic agent to the cerebral surface, or even extradurally, as it may lead to focal epilepsy; sulphapyridine, sulphadiazine and sulphacetamide appear, however, to be innocuous (A. C. Watt and G. L. Alexander, 1942; C. Pilcher, R. Angelucci and W. F. Meacham, 1942).

Evidence of the superiority of sulphathiazole in the treatment of acute gonorrhoea increases. As compared with a total dosage of 22 grammes of sulphapyridine given during five days, 6 grammes of sulphathiazole daily for two or three days gave 98 per cent of successes without producing toxic effects (F. J. G. Jefferiss and G. L. M. McElligott, 1943).

Sulphathiazole is considered best for the local treatment of impetigo contagiosa; sulphadiazine and sulphamethazine were disappointing. Sulphathiazole was used in 5 per cent strength either in a water-miscible cream or in a paste made with 15 per cent zinc oxide and 15 per cent starch; the vehicle made little difference to the rate of healing. (G. A. G. Peterkin and E. C. Jones, 1943.)

Succinylsulphathiazole

This compound is absorbed only to the extent of 5 per cent from the bowel, in which it is hydrolyzed to sulphathiazole. The minimum dose required is 0.25 gramme per kilogram (2 grains per pound) body weight daily; this dose is given as the initial one and is followed by one-sixth of the dose at four-hourly intervals. It has been shown to produce a dramatic reduction in the numbers of *B. coli* in the intestine and is considered to be equally effective with sulphaguanidine against bacillary dysentery, but *Streptococcus faecalis*, *Bacillus aerogenes* and *Bacillus proteus*, *Bacillus typhosus* and *Bacillus paratyphosus* are resistant to its action. It may prove to be of considerable value in the prevention and treatment of post-operative peritoneal infection but further clinical experience must be awaited (E. J. Poth and F. L. Knotts, 1942, W. M. M. Kirby and L. A. Rantz, 1942).

Sulphaguanidine

Much evidence has been gathered concerning the value of sulphaguanidine in the treatment of bacillary dysentery in the Middle East. Serious complications such as haemolytic anaemia, haematuria, jaundice or agranulocytosis are uncommon and rapid clinical improvement occurs with relief of pain and tenesmus, less frequent passage of stools and disappearance of blood and mucus from the faeces. The ideal treatment is administration of sulphaguanidine in every clinical dysentery case while bacteriological proof is awaited. Experience with Shiga antiserum was disappointing except in combating symptoms of exotoxin absorption (N. H. Fairley and J. S. K. Boyd, 1942¹). Further evidence favours the prompt administration of this compound in acute dysentery; delay involves more lengthy treatment, and when the stools are very frequent and loose, opium, bismuth and chalk, or kaolin should be prescribed to reduce the frequency of the stools and thus increase the concentration of sulphaguanidine in the bowel. In acute cases 7 grammes of sulphaguanidine was given at first and followed by 3.5 grammes at four-hourly intervals until two days after the stools were normal; patients with Shiga infection received 30,000 units of antiserum. In chronic cases five daily doses of 3.5 grammes were given for a minimum period of eight days. Toxic symptoms were rare and occurred in constipated patients, probably

on account of the high concentration of the drug in the bowel; the effects produced were headache, slight fever, nausea, erythema and tachycardia (A. E. Brewer, 1943).

In a comparison of cases of bacillary dysentery in the Middle East in which patients were treated either by salines with when necessary sulphaguanidine, by sulphaguanidine alone, by sulphapyridine and by kaolin, it has been shown that the average stay in bed was respectively 12·6, 5·36, 4·5 and 6·1 days; it is concluded that sulphapyridine possesses advantages over sulphaguanidine in bacteriostatic power although it is more likely to cause agranulocytosis. With sulphonamide therapy recovery is more rapid, solid food can be taken earlier and convalescence is shorter (J. W. Paulley, 1942).

The value of sulphaguanidine is endorsed by a War Office Report stating the outstanding features to be increased feeling of well-being within from twenty-four to forty-eight hours, rapid relief of pain and tenesmus and remission of abdominal symptoms, a fall in temperature and pulse rates to normal in from one to three days, remarkable reduction within five or six days of the number of the stools to only one or two daily, and rapid disappearance of blood, more slowly of mucus, from the stools. If treatment is begun within twenty-four hours of the onset less damage to the colon and more rapid recovery may be anticipated (N. H. Fairley and J. S. K. Boyd, 1942²).

Sulphaguanidine has also been proved to be of value in eradicating dysentery bacilli from the stools in dysentery carriers; dosage of 12 grammes daily for an average period of four days usually sufficed (L. A. Rantz and W. M. Kirby, 1942). Children with Sonne dysentery were effectively treated with sulphaguanidine, which also cleared the organisms from symptomless carriers (Monthly Bull. Emerg. Pub. Health Lab. Serv., 1942).

Sulphamethazine

This is 2-(4'-aminobenzenesulphonylamino) 4 : 6-dimethylpyrimidine (sulphamethazine). Dose: initial, 4 grammes (60 grains) followed by 2 grammes (30 grains) every six hours. A 33 per cent solution of the sodium salt is suitable for intravenous injection. Clinical experience in children with broncho-pneumonia and cerebrospinal fever has shown that satisfactory results have been obtained within thirty-six hours and has confirmed that the drug has a low toxicity. Dosage for children from two and a half to thirteen years of age was 4·2 grammes in the first twenty-four hours, which gave an average blood concentration of 16·5 milligrams per cent. Sulphamethazine was regarded as better than sulphapyridine because of its low toxicity, easier oral administration and longer intervals between doses (P. A. Jennings and W. H. Patterson, 1942).

Sulphadiazine

Sulphadiazine is more slowly and less completely absorbed than sulphathiazole or sulphamidamide; relatively less acetylsulphadiazine is formed and as it is more soluble renal complications are uncommon, excretion of sulphadiazine is however slower and it is thus more easy to maintain an effective concentration in the blood. Initial oral dosage of 0·1 gramme per kilogram ($\frac{3}{4}$ grain per pound) body weight is advised in pneumonia, followed by doses of 1 gramme (15 grains) every four hours until the temperature has been normal for seventy-two hours. In children, after an initial dose of 0·1 gramme per kilogram ($\frac{3}{4}$ grain per pound) body weight, one-quarter of this dose is given at six-hourly intervals. Severe infections with streptococci, meningococci or Friedländer's bacilli, require intravenous dosage of 0·1 gramme per kilogram ($\frac{3}{4}$ grain per pound) of the sodium salt in 5 per cent solution in distilled water and this is followed by oral dosage of 1 gramme (15 grains) every four hours (Council on Pharmacy and Chemistry, 1942).

NOTES ON OTHER DRUGS

Promanide

Promanide is the sodium salt of *pp'*-diaminodiphenylsulphone-N,N'-di-(dextrose sulphonate) (promin). The early successful results of chemotherapy in experimental tuberculosis have been confirmed, but while the guinea-pig tolerates a daily oral dosage of 0·3 gramme (5 grains) of promin, a much smaller dose relative to weight in man produces toxic effects, particularly in the form of haemolytic anaemia. Details of trials in pulmonary tuberculosis are not yet available, but satisfactory results by local application to superficial tuberculous lesions are reported. Promin is very soluble and is rapidly absorbed, therefore the drug was incorporated in a medium which would

limit diffusibility; the medium employed was a 3 or 3.5 per cent tragacanth gel containing 5 per cent promin. In cases of closed tuberculous abscesses and open sinuses from which cultures of human type have been grown, the patients usually have been treated by injection of 5 cubic centimetres of the promin jelly and the successful results merit extension of the clinical trials. Attention is being directed to the possibility of treating softened cervical glands by injections (W. H. Tytler and A. D. Lapp, 1942; W. H. Feldman, H. C. Hinshaw and H. E. Moses, 1940, 1941 and 1942; T. F. Jarman, 1943).

Penicillin

From crude penicillin by means of solvents and reduction a barium salt of purified penicillin has been obtained which inhibits growth of *Staphylococcus aureus* in dilutions of 1 in 24 to 30 millions; but it is unstable and inactivated by boiling or by acids and alkalis, although stable as the dry barium salt. It is relatively innocuous to leucocytes and by injection to mice. It is hoped, if the structural formula can be ascertained, that more simple methods of preparation can be found (E. P. Abraham and E. Chain, 1942; E. Chain, H. W. Florey and M. A. Jennings, 1942).

In experimental *Cl. Welchii* infections in mice, comparisons were made between the effects of zinc peroxide, proflavine, penicillin, gramicidin and sulphonamides. Zinc peroxide, active *in vitro*, was valueless on tissues; proflavine was more valuable than sulphathiazole and as effective as sulphathiazole; penicillin was still more efficacious; gramicidin gave poor results (J. McIntosh and F. R. Selbie, 1942). Other bactericidal substances, for example tyrocidin, pro-actinomycin and claviformin, have been isolated from bacteria and fungi, but those named, on account of their toxicity to leucocytes and upon injection, are unlikely to prove of therapeutic value.

Recently a number of patients have been under treatment with salts of penicillin. A reasonably stable impure sodium salt of penicillin has been obtained which is hygroscopic and which is destroyed by boiling and by acids, alkalis and oxidizing agents, but which is suitable for injection. The calcium salt is not hygroscopic and can be used locally as a powder or solution but it should not be injected intramuscularly or intravenously in strong solution. It is emphasized that penicillin is bacteriostatic but not bactericidal in therapeutic concentrations and that the body defences must be relied upon to destroy the bacteria present while penicillin prevents their multiplication. Oral administration in enteric capsules or by duodenal tube was found to be not very satisfactory. The dosage was 10,000 units every four hours by mouth in a case of facial and orbital cellulitis and 10,000 to 20,000 units by duodenal tube in a case of actinomycosis of the lung. Intramuscular injections in a child two months old of doses from 250 to 1,000 units every four hours and two intravenous injections of 2,000 and 3,000 units during a period of twenty days controlled a staphylococcal osteomyelitis without causing toxic effects. In a case of pelvic abscess intravenous dosage of 35,000 to 40,000 units in 10 cubic centimetres at twelve-hourly intervals during four days did not maintain a constant bacteriostasis in the blood, although there were no ill effects. A boy suffering from chronic osteomyelitis improved when intramuscular doses of 9,000 units in 1 cubic centimetre were given at six-hourly intervals. In acute staphylococcal osteomyelitis, doses of 20,000 units at six-hourly intervals were inadequate to maintain bacteriostasis but doses of 10,000 units three-hourly or 15,000 units four-hourly were regarded as having abolished the infection. Staphylococcal pyaemia responded initially to intravenous and later to intramuscular doses of from 20,000 to 25,000 units at three-hourly intervals. After the pus was aspirated, intrapleural injection of 10,000 units daily for twenty-four days followed by doses of 20,000 units given intramuscularly every three hours induced considerable clinical improvement and the pus became free from streptothrix after ten days and from streptococci on the twenty-fourth day. In a fulminating case of staphylococcal cavernous sinus thrombosis the condition responded after three days to intravenous and intramuscular doses of 20,000 units every three hours. Staphylococcal osteomyelitis and pyaemia were treated in a similar way. Uninterrupted recovery in an apparently hopeless case of streptococcal meningitis was made after intramuscular doses of 10,000 to 20,000 units at two-hourly intervals and 5,000 units intrathecally after the seventh day had been given. Very satisfactory clinical results were achieved in *Staph. aureus* septicaemia and osteomyelitis with pyaemia. Temporary improvement only was the result when penicillin was used in subacute bacterial endocarditis (*Streptococcus viridans*). It is concluded that intramuscular administration is the most practicable method of use,

but owing to the rapid renal excretion of penicillin, doses of at least 15,000 units should be given every three hours.

Local use of the sodium or calcium salt has been made with successful results to treat mastoid infections by the injection of a solution (250 to 500 units per cubic centimetre) every six hours; eye infections by means of a watery solution or ointment (600 to 800 units per gramme of Vaseline); and chronic wound sinuses and other septic local conditions by application of the salt. In most cases, after adequate treatment, staphylococci and streptococci were eliminated, with subsequent healing. Penicillin is as yet available only in the smallest quantities and not for general supply (M. E. Florey and H. W. Florey, 1943).

Gramicidin

Hotchkiss and Dubos (1940) from an aerobic soil organism, *Bacillus brevis*, obtained an extract termed tyrothricin, which was toxic to Gram positive cocci. This extract contains two bactericidal principles: gramicidin, which is very toxic to Gram positive organisms, and tyrocidine, which is less effective on some Gram positive and Gram negative organisms. Gramicidin is a crystalline polypeptide relatively insoluble in water but soluble in alcohol and acetone; its activity is lowered by cephalin, it reduces surface tension and it has a haemolytic action when injected intravenously. Gramicidin seems likely to be of value only when applied or injected locally or when used by irrigation, unless water soluble derivatives without haemolytic action can be obtained. *In vitro* tests show gramicidin to be intensely toxic to pneumococci and haemolytic streptococci. Clinical trials have demonstrated its value locally in eradicating Gram positive cocci and in treating chronic ulcers, maxillary sinusitis, dermatitis, wound infections, pneumococcal empyemas and chronic cystitis. By using glycerin and alcohol a solution for local application has been prepared and found effective in streptococcal but not in staphylococcal infections (W. E. Herrell and Dorothy Heilman, 1941¹, 1941², 1941³; L. S. Goodman, 1942; A. E. Francis, 1942; H. J. Robinson and H. Molitor, 1942).

Propamidine

Aromatic diamidines have been found to possess trypanocidal activity, the most active being 4 : 4'-diamidinostilbene, 4 : 4'-diamidinodiphenoxypropane and 4 : 4'-diamidinodiphenoxypentane (E. M. Lourie and W. Yorke, 1939). These compounds in dilute solutions have been found to be bacteriostatic, particularly towards Gram positive cocci but less so towards anaerobic Gram positive bacilli and Gram negative bacilli; their action is not inhibited by pus, tissue fluids or *p*-aminobenzoic acid. Propamidine (4 : 4'-diamidinodiphenoxypropane hydrochloride) proved by *in vitro* experiments to have a bactericidal as well as a bacteriostatic effect in weak concentrations varying from about 1 : 128,000 to 1 : 256,000 for *Staph. aureus* and from about 1 in 1 to 2 million for *Streptococcus pyogenes*. Against some strains of *Staph. aureus* it was more effective than sulphathiazole. Strengths of 0.1 per cent do not impair phagocytosis or cause haemolysis.

For clinical trial propamidine (0.1 per cent) was used in a watery gel containing 4.5 and 5 per cent methyl cellulose. This was used to fill up the wound, the skin edges being left dry and the wound and skin covered with impermeable Vaseline gauze; re-dressing was done usually on alternate days. Concentrations above 0.1 per cent may injure granulations and even this strength may irritate the skin at the edges of the wound. Propamidine can clear a wound of organisms within ten days; longer applications may cause a mild superficial necrosis. Streptococci disappear first, then staphylococci, but *Proteus vulgaris* and *Pseudomonas pyocyanea* often persist without retarding progress of healing. After ten days' application, secondary excision or skin-grafting has the best chance of succeeding. Some fifty cases (mainly of chronic wound sepsis) have been treated with satisfactory results (W. R. Thrower and F. C. O. Valentine, 1943).

Confirmatory evidence of the value of propamidine jelly in eradicating persistent β -haemolytic streptococcal infections within four to ten days and after other methods had failed is afforded from a series of eleven cases in which the patients were undergoing plastic treatment (A. H. McIndoe and A. R. Tilley, 1943). Clinical trials have also been made in burns with a 0.1 per cent propamidine in a Mumford (lanette wax SX) base, with a 0.05 per cent propamidine in the original jelly base and with a 'first-aid' preparation of 0.1 per cent propamidine with 1 per cent amylocaine hydrochloride in the Mumford base. The last preparation was regarded as simple to apply, extremely

soothing and almost ideal for first aid. The progress of patients was remarkable for speed of slough separation and of epithelial repair with a minimum of scar tissue and with good cosmetic and functional results. Propamidine fails to control *B. proteus* and *Ps. pyocyanea* infections, which must be controlled by other measures before skin-grafting can be done with safety (G. H. Morley and J. P. Bentley, 1943). Similar satisfactory results have been recorded in treating leg ulcers, wounds and burns (F. Kohn, M. H. Hall and Clara D. Cross, 1943).

Dicoumarin

Dicoumarin, 3 : 3'-methylene-bis-(4-hydroxycoumarin), occurs as white crystals slightly soluble in water but readily soluble in alkalis. Dicoumarin is an anticoagulant and has been suggested as a substitute for heparin (see Surveys and Abstracts 1940, p. 136). Heparin acts quickly but only for a short time both *in vitro* and *in vivo* and its effect can be annulled by protamine. The action of dicoumarin is delayed for from twenty-four to forty-eight hours, whether given orally—when the effects are irregular owing to uneven absorption—or intravenously (as the disodium salt). It causes a prolonged fall in the prothrombin concentration, lasting usually from three to seven days; the only antidote is fresh blood given by transfusion; vitamin K or menaphthone is of no use. The initial oral dose is 0.2 to 0.3 gramme (3 to 5 grains) but further doses should be controlled by the prothrombin time which, if above thirty-five seconds for undiluted and ninety seconds for 25 per cent diluted plasma, indicates that the drug should be withheld. Dicoumarin has been recommended for the prevention of post-operative embolism and thrombosis and in the treatment of thrombophlebitis. Dicoumarin does not at present appear to possess any advantages over heparin (E. V. Allen, N. W. Barker and J. M. Waugh, 1942; C. S. Davidson and Harriet MacDonald, 1943).

TREATMENT OF SCABIES

Conflicting opinions continue to be expressed upon the ideal treatment for scabies. A comparison of the common methods in use is given by K. Mellanby, C. G. Johnson and W. C. Bartley (1942), and they conclude that only sulphur ointment and benzyl benzoate are satisfactory. Benzyl benzoate lotion (benzyl benzoate 25, soft soap 35, spirit 40) was found to be one hundred per cent effective and the following three emulsions proved successful. (1) benzyl benzoate 20 cubic centimetres, lanette wax SX 1 gramme, water 80 cubic centimetres; (2) benzyl benzoate 20 cubic centimetres, stearic acid 2 grammes, triethanolamine 0.5 cubic centimetre, water to 100 cubic centimetres, (3) benzyl benzoate 20 cubic centimetres, 1 per cent solution of cellofas WFZ 80 cubic centimetres.

Tetraethylthiuram monosulphide (T.E.T.M.S.) was suggested by R. M. Gordon and D. R. Seaton (1942¹), (1942²) as the result of experiments on rats infected with itch mites. G. H. Percival (1942) showed that in 5 per cent aqueous solution it was curative in fifty consecutive cases of scabies. T. M. Clayton (1943) used a solution of tetraethylthiuram monosulphide 25 in polyglycerol ricinoleate 10 and industrial methylated spirit 65; this did not produce any dermatitis in controls. After a bath and scrub the patient was dried and the monosulphide emulsion rubbed thoroughly over the body; raw or septic areas were covered with lint soaked in the emulsion. Treatment was given at three-day and four-day intervals and three or four applications were sufficient. The results showed that prompt relief was given from itching and that there was improvement in the patient's general health.

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ABDOMINAL PAIN AND ACUTE ABDOMINAL EMERGENCIES

See also B.E.M.P., Vol. I, p. 1; and Cumulative Supplement, Key Nos. 1-11.

Diagnostic significance of pain*Referred pain*

Reno-ureteral disease and reflex abdominal pain.—In a paper read at a Staff Meeting of the Cedars of Lebanon Hospital, Los Angeles, L. Gunther and S. Reznick discuss the relation between reno-ureteral disease and reflex abdominal pain. They have studied a group of patients complaining of abdominal pain without objective findings and maintain that careful analysis of the distribution of the pain and the order of its evolution will enable the clinician to determine its origin. Most abdominal pains are distributed according to one of two patterns: radicular pain has its origin in the spinal nerve roots and is segmental in distribution; pain resulting from visceral disease is not strictly segmental in distribution, occupying only part of each of the dermatomes to which it is projected. At no time is the entire zone of any one dermatome completely involved; the pattern is a broken one occurring within the primitive pattern of root pain. The differential diagnosis is often difficult owing to the fact that various viscera receive their nerve supply from the same spinal segments. Reno-ureteral disease may be associated not only with the classical pain of renal colic but with one or more of four reflexes, reno-gastric, reno-intestinal, reno-hepatic and reno-peritoneal. Pain occurs in the distribution of the ninth dorsal to first lumbar spinal segments and shows the characteristic features of non-radicular pain outlined above. In accordance with the rule that pain from centrally placed viscera is projected towards the midline and pain from laterally placed viscera laterally, the pain in reno-ureteral disease is usually felt towards the side corresponding to the affected kidney.

Diagnosis of acute abdominal emergencies*Conditions simulating acute appendicitis*

Analysis of a hundred cases.—N. Rosenberg analyses a series of 100 cases wrongly diagnosed as acute appendicitis and explored on that diagnosis. This author maintains that the risk of delay in genuine appendicitis amply justifies early exploration in the doubtful case. Of this group of patients, 83 per cent were under thirty and 60 per cent were under twenty years of age. A large majority (69 per cent) was of the female sex. Previous attacks of abdominal pain had occurred in 38 per cent of the patients. Generalized or midline abdominal pain with subsequent shift to the right lower quadrant was described by only forty-four of the patients; in an additional twenty-one generalized or midline pain occurred without a shift to the right lower quadrant. In eighty-eight right lower quadrant pain was present at some stage of the illness. Nausea occurred in fifty-four cases and vomiting in forty-nine. Rectal tenderness was found in sixty-five cases. Leucocytosis of over 10,000 per cubic millimetre was present in forty-three of seventy-two patients whose white cell count was done. A diagnosis of appendicitis had been made in seventy-seven instances by the doctor sending the patient to hospital. In the remaining cases the diagnosis had been queried. In 55 per cent some other recognizable pathological condition was found to account for the 'acute appendix syndrome'. The rest could not be satisfactorily explained at laparotomy, two were subsequently found to have gall-stones and one developed ileo-caecal tuberculosis. The pathological conditions found in the above fifty-five patients included (1) acute mesenteric adenitis in seventeen cases; (2) acute ovarian conditions (rupture of a Graafian follicle or corpus luteum cyst) in sixteen cases, in thirteen of which the right ovary was affected, and in three the left; (3) tubal inflammation in three cases, and (4) miscellaneous lesions (acute regional ileitis, Meckel's diverticulitis, and so on) in ten cases.

Need for careful evaluation of symptoms.—Urging that careful consideration is necessary before appendicectomy is advised in cases of recurrent right lower abdominal pain, G. J. Willauer and J. F. O'Neill present the histories of 375 patients treated by appendicectomy. Of 255 appendices examined microscopically 104 did not show any evidence of disease, whereas in the entire series only twenty-one were regarded as normal at operation. The discrepancy is accounted for by the fact that many of the appendices were found to be obstructed as a result of faecoliths or kinking and that such obstruction can give rise to pain. The patients' ages varied from one to thirty-nine years, the largest number falling into the age group of ten to nineteen years. The ratio of females to males was 1.6 to 1. A history of at least one previous attack was given by 85 per cent of the patients. Pain was the chief symptom in all but one of the cases. In 51.7 per cent it occurred in the right lower quadrant only. Nausea, vomiting, or both, occurred in 64.8 per cent. In most cases the leucocyte count was not raised; in only 16.6 per cent was it above 10,000 per cubic millimetre. Enlarged mesenteric glands were reported in nine cases. Pathological changes in other abdominal viscera were found in thirty-two cases. No deaths occurred in this series. Inquiries after operation revealed that 74.4 per cent of the patients were free from symptoms; 111 complained of abdominal discomfort or pain, which in twenty-seven appeared to be exactly the same as before the operation. Of these twenty-seven patients, nineteen were women, eight of whom suffered from irregular and painful menstruation, which suggests that there was some endocrine dys-

function. Three of the patients were very poorly nourished and four turned out to be neurasthenics. Greater consideration should probably be given to endocrine and nutritional factors in cases of this kind.

Acute intussusception

Aetiology and clinical picture.—P. G. Rowe, who reports ten cases, points out that intussusception is very rare after the age of fourteen. The majority of intussusceptions in adults are secondary; in Rowe's series two were primary; the remainder were secondary to other conditions, including Meckel's diverticulum and growth. Two were of the retrograde type; in one the ileum was involved, in the other the jejunum had entered the stomach through a gastro-jejunostomy. The ages of the patients ranged from fifteen to fifty-eight. Four subjects were females, six males. In two cases the illness was acute, in the remainder chronic, although in two of the chronic cases acute symptoms developed just before operation. Two patients died after operation. The diagnosis in adults is often difficult and may be possible only when the abdomen is opened. An abdominal mass was felt in only two of the patients in the above series; in one the intussusception was palpable per rectum.

Rarer causes of intestinal perforation

Foreign bodies.—G. O. Chambers has operated in sixteen cases of swallowing of foreign bodies by inmates of prisons. The intentional swallower is usually a psychopathic person and in restraint becomes stubborn and antisocial. Operation is performed only after six weeks' palliative treatment under X-ray control, unless symptoms supervene. In eight patients (50 per cent) of the present series the bowel was perforated by the time the patient came to operation. No case of perforation of the stomach was encountered. All the eight cases presented signs of an acute abdominal lesion. The widest article to pass the pylorus and the ileo-caecal valve measured one inch in diameter. No fork or dessertspoon got beyond the stomach; the longest article to traverse the duodenum and ileo-caecal valve measured $5\frac{1}{2}$ inches; most of the foreign bodies were found in the colon. One patient died, a mortality of 6.25 per cent.

Chambers, G. O. (1942) *Brit. med. J.*, **2**, 362.

Gunther, L., and Reznick, S. (1943) *Urol. cutan. Rev.*, **47**, 6.

Rosenberg, N. (1942) *Amer. J. Surg. N.S.*, **58**, 365.

Rowe, P. G. (1942) *Canad. med. Ass. J.*, **47**, 219.

Willauer, G. J., and O'Neill, J. F. (1943) *Amer. J. med. Sci.*, **205**, 334.

ABORTION

See also B.F.M.P., Vol. I, p. 47; and Cumulative Supplement, Key No. 12.

Natural and unintentional abortion

Causes

Experiments with artificial pyrexia—J. A. Cameron has investigated the effect of artificial pyrexia in early pregnancy. Twenty matings were made in fourteen doe rabbits, and seventy-two to eighty hours afterwards, each was given fever treatment by means of a bath of hot water in which the animal was kept until its temperature had stood at 108° – 109° F. for twenty minutes. Seventeen of the matings did not result in any litters; of the three rabbits which produced normal offsprings two had for different reasons received inadequate treatment. Of ten animals subsequently mated eight produced litters. The author draws the inference that fever can terminate early pregnancy in the rabbit.

Cameron, J. A. (1943), *Proc. Soc. exp. Biol. N.Y.*, **52**, 76.

ACANTHOSIS NIGRICANS

See also B.F.M.P., Vol. I, p. 75; and Cumulative Supplement, Key No. 14.

Clinical picture

Urticarial character

Obstinate nature of disease.—A. G. Franks reports a case of acanthosis nigricans associated with urticaria: an unmarried soldier, twenty-nine years old, was admitted to hospital with an eruption of two months' duration, associated with itching and burning which increased in warm atmospheres. The appearance of an erythematous and urticarial eruption had been noted after injections of tetanus toxoid, and acanthosis nigricans subsequently supervened. The family history was negative. Physical examination revealed a patch of unknown character, possibly a developmental defect, at the margin of the left optic disk. Beyond that and the skin condition no abnormalities were found. The eruption involved the neck, axillae, forearms, abdomen, nipples and perineum. The involved areas showed furrowing and pigmentation, papillary hypertrophy and in places papillomatous growths. Urticarial wheals were present. The nails did not show any change. The tongue was rough and slightly darkened. A section of the skin revealed moderate hyperkeratosis, acanthosis, subepithelial oedema and hypertrophy of the granular layer and papillary bodies. The suggestion is made that the tetanus toxoid caused damage to some part of the endocrine system and led to the development of acanthosis nigricans. Treatment of the urticaria during a period of five months by elimination diets, epinephrine, liver extract, calcium and autohaemotherapy has been unavailing.

Franks, A. G. (1943) *Arch. Derm. Syph., N.Y.*, **47**, 97.

ACCESSORY SINUSES OF THE NOSE

See also B.E.M.P., Vol. I, p. 77; and Cumulative Supplement, Key Nos. 15–17.

The accessory sinuses of the nose*Acute sinusitis*

Sulphathiazole microcrystals.—The use of microcrystals of sulphathiazole in otolaryngology is discussed by L. E. Silcox and H. P. Schenck, who have used them in the treatment of a group of 130 patients suffering from sinusitis, acute infections of the upper respiratory tract and otitis media, and in a small number of mastoidectomy and other cases. All the drugs of the sulphanilamide group, except sulphadiazine, are said to be in crystals of such size or shape that they will not pass through the barrel of a fine needle. Violent agitation, produced by intense sound waves or by other means, during neutralization of an alkaline solution of the drug has been found to result in the formation of crystals so small that, in a neutral suspension, they pass readily through a size 26 hypodermic needle. When such a suspension was injected into a rabbit's antrum it was found that a film of microcrystals was deposited on the mucous membrane; no signs of irritation were seen, and sections did not show any foreign-body reaction such as often occurs with sulphathiazole powder. Various concentrations of the drug were tried, and the optimum was found to be 5 per cent, which was used in all the patients in the present series. In the cases of acute infection of the nose and paranasal sinuses the drug was combined with parendrine 1 per cent in order to reduce oedema and to allow the suspension to reach all parts of the infected area. Toxic manifestations were not observed in any of the patients, and the local results were encouraging. Thus, in eighteen patients with acute sinusitis of one antrum, the average period before the washings became sterile was three days, and a positive culture was not obtained subsequently in any case. In fifty-two patients with acute and chronic sinusitis the results were uniformly good. Twenty-seven patients with common colds were treated within twenty-four hours of the onset, and another control group of twenty-two was treated by ordinary methods. In the treated group all the patients experienced relief of symptoms, and only one developed complications (epistaxis and bronchitis). In the control group epistaxis was noted four times, bronchitis eleven times and otitis media twice.

Silcox, L. E., and Schenck, H. P. (1942) *Arch. Otolaryng.*, Chicago, **36**, 171.

ACHALASIA

See also B.E.M.P., Vol. I, p. 116; and Cumulative Supplement, Key No. 18.

In the alimentary tract*Of the cardiac sphincter*

Cardiospasm, or achalasia of the oesophagus—In the course of a review of 'the mechanism of swallowing', V. E. Negus discusses the problems of cardiospasm and achalasia of the lower end of the oesophagus. He points out that although many authors refer to a sphincter at the lower end of the oesophagus and the accounts vary, there is general agreement that the sphincter is very feeble and that it is not at all comparable to the sphincters of the urinary bladder and rectum. He has never seen, on direct oesophagoscopy, any evidence of its existence, but considers that a somewhat neglected factor has been the difference in physical conditions to which the thoracic and abdominal segments of the oesophagus are subjected. Normally in the thorax there is reduced pressure which tends to open the oesophagus, whereas in the abdomen the pressure is raised, causing mutual apposition of the viscera and closing of the abdominal oesophagus. The address was followed by a discussion in which A. Hurst described the history of cardiospasm and achalasia, going back to Thomas Willis in 1672. Hurst regards every case of megaesophagus as being due to want of relaxation, or achalasia (*a* – not, and *γῆλασις* – relaxation) a term suggested, at Hurst's request, by the late C. Perry. Hurst's treatment by the passage of mercury bougies is the outcome of his studies on achalasia, which he ascribes to atrophy or degeneration of Auerbach's (myenteric) plexus, a condition shown to be present in each of forty-one cases which were investigated by other workers. J. Walton's clinical experience of nearly fifty cases of cardiospasm was entirely in disagreement with that of Hurst's in achalasia, and his treatment was correspondingly different, namely gastrostomy and digital dilatation of the lower end of the oesophagus.

Hurst, A. (1942) *Proc. R. Soc. Med.*, **36**, 93.

Negus, V. E. (1942) *Proc. R. Soc. Med.*, **36**, 85.

Walton, J. (1942) *Proc. R. Soc. Med.*, **36**, 95.

ACNE

See also B.E.M.P., Vol. I, p. 156; and Cumulative Supplement, Key No. 23.

Acne vulgaris*Treatment*

X-irradiation.—P. R. Kline and E. Gahan have investigated the action of X-ray treatment in fifty patients with acne vulgaris. Irradiation was given to one side of the face only, the other side being treated by ordinary methods. The dosage of X-rays was 75 r, unfiltered, at weekly intervals; the average number of treatments was ten. Thirteen of the patients ceased to attend before the course was completed; one developed erythema for which treatment was discontinued and one had rosacea and did not show any improvement. In twenty cases the

untreated side improved as much as the treated side; in nine cases improvement was seen only on the treated side; in six no improvement occurred. The effect on the untreated side suggests some humoral as well as a direct local action of the rays. In three patients erythema appeared on both sides of the face and persisted for several weeks. Scarring was not any greater on the treated than on the untreated side.

Kline, P. R., and Gahan, E. (1942) *Arch. Derm. Syph., N.Y.*, **46**, 207.

ACROMEGALY

See also B.E.M.P., Vol. I, p. 166; and Cumulative Supplement, Key No. 24.

Treatment

Oestrogens

Clinical results —E. L. Hutton and M. Reiss report four cases, three of well developed and one of incipient acromegaly, all treated according to the method originated by Zondek (1936), namely by the degeneration of the growth-promoting and gonadotrophic cells of the anterior pituitary lobe. This degeneration was induced by oestrogens, of which large doses were required. The following changes were found after treatment: decrease in size of the thickened phalangeal joints; extremely rapid improvement of the subjective symptoms, headache, giddiness and amblyopia; visual improvement, depending entirely upon the degree of optic atrophy present before the beginning of the treatment. The main drawback of the treatment is the high oestrogen dosage necessary, which profoundly influences gonadal function.

Hutton, E. L., and Reiss, M. (1942) *J. ment. Sci.*, **88**, 550.

ACTINOMYCOSIS

See also B.E.M.P., Vol. I, p. 173, and Cumulative Supplement, Key No. 26.

Treatment

Radical surgical eradication

Clinical results —In the treatment of actinomycosis early diagnosis is of the greatest importance. O. S. Randall, who advocates complete surgical eradication of the diseased area as the treatment of choice, points out that such extirpation is possible only in early cases, and urges that actinomycosis should be considered as a possibility in any suppurative process involving the head or neck and which is of more than two weeks' duration. The diagnosis is made by microscopical examination of pus or scrapings from the abscess cavity. Randall describes sixteen cases, one fatal; three of the remaining cases have not been adequately observed subsequently. The other twelve patients have not relapsed for periods of from four to ten years. Some patients required several operations to eradicate all the diseased tissue. In some cases diathermy excision was used, while in other cases curetting was performed. X-ray therapy and potassium iodide were given in some cases, in addition to surgical treatment; the author regards them as useful adjuvant measures. The cervico-facial form of actinomycosis carries a much more favourable prognosis than does actinomycosis elsewhere in the body, owing to its accessibility and to the likelihood of early recognition. The same principle of radical surgical treatment applies to actinomycosis of the thorax and abdomen, but most patients come too late for such ideal to be realized. The disease is not rare in children; three of the patients in the present series were under fifteen years old.

Randall, O. S. (1942) *Amer. J. Surg. N.S.*, **57**, 433

ADRENAL GLAND DISEASES

See also B.E.M.P., Vol. I, p. 232, and Cumulative Supplement, Key No. 30.

Hyperfunction of the adrenal cortex: hyperplasia and neoplasm

Morbid anatomy

Desoxycorticosterone acetate and nephrosclerosis.—H. Selye, in further observations subsequent to his experiments, which showed that testicular hormones, especially testosterone and its close derivatives, exert a serotrophic effect, records experiments on twelve three-day-old single-combed white leghorn chicks treated by subcutaneous injections of 0.5 milligram of desoxycorticosterone acetate in 0.05 cubic centimetre of peanut oil twice daily; as controls twelve similar chicks were given 0.5 milligram of cholesterol, a pharmacologically inert steroid. After about ten days the chicks injected with desoxycorticosterone acetate began to drink more water than did the controls, and showed some tissue oedema. On the twentieth day of the experiment six of the chicks in each series were killed. The organs of the control chicks were normal. In the others, ascitic, pericardial and subcutaneous effusions, large white kidneys, hypertrophy of the heart (particularly of the left ventricle) and thickening of the aorta and its main branches were found. Microscopically, the renal tubules were dilated and both the parietal and the visceral laminae of Bowman's capsule showed hyperplasia. These experiments show that in young chicks overdosage with desoxycorticosterone acetate may produce typical nephrosclerosis accompanied by cardiac dilatation and hypertrophy, tissue oedema, ascites and pericardial effusion. It is pointed out that adrenal cortical tumours are often accompanied by hypertension and that after extirpation of the tumour the blood pressure returns to normal. It is very tentatively suggested that adrenocortical involvement may cause nephrosclerotic hypertension. The effects of overdosage of desoxycorticosterone acetate in cases of Addison's disease are mentioned.

Inclusion bodies in multiple carcinoma.—R. J. Stein records a case in a white woman, aged fifty-eight, of multiple primary carcinoma of the mamma, rectum and adrenal gland, in which the left adrenal gland contained a characteristic primary papillary carcinoma and numerous intracellular inclusion bodies which corresponded closely to the inclusion bodies of the virus diseases.

Hyperfunction of the adrenal medulla

Symptoms

Phaeochromocytoma.—Two cases of phaeochromocytoma are reported by E. P. McCullagh and W. J. Engel. The first patient, a girl aged nineteen, had suffered for six months from attacks, occurring from fifteen to twenty times a day, in which she experienced a feeling of intense heat, sometimes associated with dizziness and faintness and quickly causing drenching perspiration of the face and body; the hands and feet remained cold and clammy. During the attacks she was conscious of pounding of the heart and tremor of the whole body. She was admitted to hospital for investigation. While she was under observation the blood pressure was variable, usually being high, but it was not higher during the attacks; there was persistent tachycardia; the basal metabolic rate was raised, the fasting blood sugar was 128; the urea clearance test was very high. An adrenal tumour could not be demonstrated by plain X-ray examination or by intravenous urography, but the symptoms were considered to be sufficiently suggestive to warrant abdominal exploration. The right side was explored first, because adrenal tumours seem to be more common on the right side. Even before seeing the tumour the surgeon was convinced of its presence because manipulation in the suprarenal area was followed by a rapid rise of blood pressure, both systolic and diastolic. The tumour was dissected from the adrenal gland, which was left intact. As soon as the vessels were ligated the blood pressure fell sharply. Plasma transfusion was begun and adrenaline was given in repeated doses. The patient made a good recovery. The tumour measured 5.5 × 4.3 × 3.5 centimetres; it was encapsulated and showed a microscopic structure identical with that of adrenal medullary tissue. The second patient, a man aged twenty-eight, complained of weakness and tremor of two weeks' duration, and of extreme frequency of micturition which had lasted for a year. His face was very red, the blood pressure was 174/104 millimetres Hg, and he had a nodular goitre. The fasting blood sugar was 246 milligrams per cent and the basal metabolic rate was plus 36. A diagnosis of toxic goitre was made and, after a period of preparation, subtotal thyroidectomy was performed. The man developed cellulitis of the face on the fourth day and died on the fifth day after operation. Necropsy showed a phaeochromocytoma of the right adrenal gland, 16 centimetres in diameter, and a second similar tumour, 1.5 centimetres in diameter, lying on the aorta at the level of the renal arteries. In neither case did classical hypertensive attacks occur. The increased blood flow through the tissues is thought to account for the raised basal metabolic rate and for the high urea clearance in case 1, and possibly in part for the polyuria in case 2. The urea clearance test may prove to be of diagnostic value in such cases.

McCullagh, E. P., and Engel, W. J. (1942) *Ann. Surg.*, **116**, 61

Selye, H. (1942) *Canad. med. Ass. J.*, **47**, 515.

Stein, R. J. (1942) *Amer. J. clin. Path.*, **12**, 630

ALCOHOLISM

See also B E M P, Vol. I, p. 280; and Cumulative Supplement, Key No. 36.

The toxic effects of alcohol

Acute alcoholism

Hypoglycaemia as a sequel—H. St. G. Tucker, Jun. and W. B. Porter report four cases of hypoglycaemia after alcoholic intoxication. One patient was later admitted for the second time. The patients were brought to hospital in coma and not in any case was it possible to determine what sort of drink had been taken, although suspicion fell upon a denaturated alcohol solvent sold locally under the name of 'solox'. The recognition of this occasional cause of unconsciousness is important because death might occur if it were not properly treated. All the patients were known alcoholics who had engaged in a recent bout of drinking and in every case unconsciousness came on from eight to twelve hours after the last known drink had been taken. Two of the patients had slept for some hours and had wakened up again before lapsing into unconsciousness. In one case convulsions occurred. All the patients were completely unconscious and none had a smell of alcohol; all had very low blood sugar values, ranging from 0.020 to 0.038; all recovered promptly when given glucose intravenously. In the later cases this was done without waiting for the report on the blood sugar. It is thought that a toxic factor, possibly one of the denaturing substances, was responsible.

Treatment of the alcoholic

Medicinal treatment and institutional control

General management and psychotherapy.—In what he calls a didactic note on alcoholism, M. Moore deplores the lack of interest in the problem often shown by orthodox medical practitioners. The alcoholic is a special kind of neurotic, sometimes being a psychotic or borderline case, and treatment is essentially a medical problem. Some characteristics of the alcoholic subject suggest that he may have an incompletely developed personality, some that he may be constitutionally or chemically abnormal, some that the tendency to drink to excess

may be the expression or the result of some deep-seated psychical disturbance. The alcoholic requires the same careful medical consideration that has been given to the diabetic patient.

Psychotherapy in chronic alcoholism.—M. M. Miller emphasizes the value in dealing with chronic alcoholism of close cooperation between the psychotherapist and the police courts. He describes his results in a series of persons who were arrested for public intoxication, most of whom had been repeatedly arrested on similar charges. All had been sentenced to three or six months' imprisonment, with the option of undergoing treatment. Those who accepted the offer were interviewed several times, physical defects were corrected as far as possible and, when satisfactory relations had been established—generally within a month—the patient's release on probation was arranged with the Court. Ambulatory treatment was begun immediately. Amphetamine sulphate, 5 to 10 milligrams ($\frac{1}{12}$ to $\frac{1}{8}$ grain), was given after breakfast and lunch, and phenobarbitone, 0.03 gramme ($\frac{1}{2}$ grain), was also administered when necessary. Patients were advised to take sweets to keep the blood sugar at an adequate level. After from four to six months' satisfactory progress, daily treatment was discontinued but the patient was supplied with amphetamine sulphate to take if the craving for drink became uncontrollable. Psychotherapy was given in the form of re-education and suggestion. Occupation and recreation were arranged. A social sense was fostered by encouraging the patient to join an abstinent group. This intensive treatment was continued for from one to six months. Subsequent observations on 487 patients at from four to fourteen months showed that 81.4 per cent were abstinent. Of 167 subjects who were observed for nine months, 25 per cent were rearrested for drunkenness as compared with 42 per cent of untreated controls. The percentage of patients receiving relief fell from 39.5 to 18 after treatment.

Treatment of acute and chronic alcoholism.—An alcoholic is defined by A. E. Carver as a person who cannot face reality without alcohol and cannot adjust himself to reality as long as he continues to take alcohol. The aim in treatment is to overcome this mental instability. Sufficient correlation has been established between the subject's behaviour and the percentage of alcohol in his blood to justify the new Swedish law that a blood alcohol content of 1.5 per 1,000 is taken as proof of unfitness to drive a car. Treatment is described under two headings. (1) Acute intoxication. The first step is to empty the stomach. Robust patients may be given apomorphine $\frac{20}{10}$ to $\frac{10}{10}$ grain (0.003 to 0.006 gramme) subcutaneously; the patient must be watched afterwards until vomiting ceases, lest in his sleepy condition he should choke. Alternatively the stomach may be washed out and in debilitated persons a pint of hot coffee may be introduced before the tube is withdrawn. For 'hangover' an intravenous injection of 5 cubic centimetres of 10 per cent cardiazol (leptazol) solution may be given. Insulin with glucose accelerates elimination of alcohol from the blood, but is best reserved for institutional practice. In methyl alcohol ('Red Biddy') intoxication, acidosis must also be combated by large injections of sodium bicarbonate solution. (2) Chronic addiction. Withdrawal should be abrupt rather than gradual, except in longstanding cases in elderly people, and even then the process should take less than a week. Paraldehyde is advisably added to the whisky used for tapering because it renders the dose unpalatable and conceals the amount of whisky it contains; it also has a sedative action. Subsequent treatment requires the patient's cooperation and is best carried out in a special institution in which a regulated mode of life, occupational therapy and physical and psychological treatment are attainable. Plenty of sugar and sweets should be allowed, and glucose may be given intravenously if necessary; insulin treatment is sometimes beneficial. A sedative is usually required at first; to avoid habituation it should be changed often and the patient should not be told what drug he is taking. Apomorphine subcutaneously in small repeated doses ($\frac{10}{10}$ grain, 0.0015 gramme) does not cause vomiting and will often ward off a threatened relapse. A single dose of $\frac{10}{10}$ grain (0.002 gramme) given last thing at night when the patient is in bed is excellent for insomnia of delayed type. Benzadrine has been found to give disappointing results, and addiction is a real danger. Hypodermic injections of strychnine and atropine are helpful. The prognosis depends chiefly upon the mentality of the patient. Abstinence is the only safe course for the susceptible individual. Patients' friends must be warned against quack remedies.

Carver, A. E. (1942) *Med. Pr.*, **208**, 295.

Miller, M. M. (1942) *J. Amer. med. Ass.*, **120**, 271.

Moore, M. (1943) *J. nerv. ment. Dis.*, **97**, 1.

Tucker, H. St. G., Jun., and Porter, W. B. (1942) *Amer. J. med. Sci.*, **204**, 559.

ALKAPTONURIA

See also B.E.M.P., Vol. I, p. 300; and Cumulative Supplement, Key No. 39.

Aetiology

Relationship of hyperuricaemia

A. Leslie, of the Mount Sinai Hospital, New York, records the first published case—that of a American housewife, twenty-four years old—of the combination of alkaptonuria and hyperuricaemia. From birth, blackening of her diapers had been noticed by her mother who had diabetes mellitus but not alkaptonuria. The patient had had osteoarthritis of the sternoclavicular joints since 1936. Her blood uric acid varied from 7.9 milligrams to 13.3 milligrams per 100 cubic centimetres when taking tincture of colchicum; improvement followed treatment by colchicum and also by ascorbic acid. In the case of alkaptonuria reported by R. B. Gibson and C. P. Howard (1921) there was moderately high urinary excretion of uric acid, but no

estimation of the blood level of uric acid was made. The author admits the temptation to speculate about a possible causal relation between the alkaptonuria and the hyperuricaemia; but concludes that there is not any connexion between the two disturbances, and laboratory work and treatment failed to support such a view.

Gibson, R. B., and Howard, C. P. (1921) *Arch. intern. Med.*, **28**, 632.

Leslie, A. (1943) *Arch. intern. Med.*, **71**, 68.

ALLERGY

See also B.E.M.P., Vol. I, p. 302; and Cumulative Supplement, Key Nos. 40–52.

General diagnosis of allergic cases and identification tests

Aetiology and pathology

Allergens in house dust.—In a paper read before the American Association for the Study of Allergy Marion T. Davidson attempts to determine the source of the allergic activity of house dust. The skin reactions of 100 subjects sensitive to house dust were tested with the common ingredients of this dust. These are cotton, flax, jute, wool, silk, six or more kinds of animal hair, three or more kinds of feather, glue, kapok, orris-root, pyrethrum and tobacco. It appears that horse dandruff is the most common producer of a reaction in patients sensitive to house dust, closely followed by cow hair and cat hair. Horse hair is used in almost all upholstered furniture and in padding for men's coats and could thus easily contaminate house dust. The use of cowhide-soled shoes may explain the frequency of reactions to cow hair. The author maintains that the presence of common allergens in house dust sufficiently explains its allergic properties.

Cross desensitization.—Kate Maunsell has studied this in susceptible people in order to obtain evidence regarding the phenomenon known as 'cross desensitization'. It has been claimed that patients sensitive to a number of allergens can be made insensitive to all by injections of one only; this means that the anti-allergic mechanism is non-specific. The intracutaneous desensitizing injections were carried out with two extracts, for example pollen and fish or feather and flour. The paired extracts were injected symmetrically on the two sides of the back, and unless the resulting reaction was intense the dose was increased 25 per cent at each successive injection. On the day after the last desensitizing injection was given each site was tested against the initial dose of its corresponding allergen, and on the following day the maximum dose was repeated in order to make sure that the level of local desensitization was maintained. Twenty-four hours later histamine was injected to determine whether the treated areas were refractory to any stimulus. This was found not to be the case. A wide range of reciprocal cross desensitization was demonstrated, and the validity of this phenomenon was thus upheld. An interesting manifestation of local cross desensitization after the injections was seen in a patient with a high degree of sensitivity to fish. He was desensitized in two skin areas for fish and in two others for feathers. He then ate two grammes of fish. An urticarial rash developed which involved the entire skin surface with the exception of the four treated areas, each about two inches in diameter, which remained unaffected.

Diagnosis

The use of dried extracts in naturalization tests.—The problem of preparing suitable extracts for testing and treating allergic patients is discussed by L. H. Criepe. The ideal extract is painless on injection and remains potent and sterile for a long time at room temperatures. Liquid extracts undergo rapid loss of potency. Glycerinized extracts are more stable but cause pain on injection and are apt to cause non-specific reactions; refrigeration delays loss of potency but is inconvenient. Dried extracts are preferable and the cryochem apparatus is a simple and practical means of preparing them. With this apparatus the frozen material is dried *in vacuo* over calcium sulphate; the residuum is redissolved in distilled water for use in suitable dilutions. The comparative potency of the extracts can be determined by various methods. The direct skin test, because it is influenced by so many factors, is the least reliable. The neutralization test is both convenient and accurate. It is performed as follows. A series of nine test-tubes is set up, and 0.2 cubic centimetre of serum from an untreated ragweed-sensitive person is placed in each tube. The extract is diluted serially from 1 in 10 to 1 in 1280 and 0.2 cubic centimetre of each dilution and of the concentrated extract is added to one of the test-tubes. To the ninth or control tube is added only normal saline. The tubes are shaken and are allowed to stand at room temperature and then the contents of each is tested intradermally in a person who is not sensitive to ragweed. Absence of a reaction shows that neutralization of the antigen in that test-tube is complete. Extracts made in the above way were found after twenty-two months to exceed greatly the potency of the corresponding saline and glycerin extracts. The hydrogen ion concentration of the extracts does not change and the risk of bacterial contamination is reduced.

Treatment

Hormones.—L. Farmer reviews the literature relating to the influence of various hormones on anaphylactic shock in animals, and finds that such influence takes the form of either enhanced or diminished reactivity and is pronounced. In a series of clinical cases of allergy he claims to have observed in human beings a similar phenomenon which appeared to be related to hormonal variations. Thus in three women, two with hay fever and one with asthma, the attacks ceased during pregnancy; in another woman attacks of angioneurotic oedema

began soon after delivery and ceased after treatment by antuitrin S. A woman with mild hyperthyroidism developed obstinate urticaria which was cured by thyroidectomy. In two women vasomotor rhinitis developed at the time of the menopause, and in one the condition was much relieved by oestrogen administration. Oestrogen was also used successfully for two women in whom allergic symptoms (urticaria and eczema respectively) coincided with menstruation.

Allergic diseases

Respiratory system

Vasomotor rhinitis.—H. H. Gelfand in a paper read at a staff meeting of the Gouverneur Hospital, New York, discusses the management of uncomplicated non-seasonal allergic vasomotor rhinitis. The condition is characterized by blocking of the nose, persistent rhinorrhoea and, in adults, paroxysms of sneezing. The mucosa is swollen and pale pinkish grey in colour and the secretions usually contain numerous eosinophil cells. An attempt must be made to establish the allergen responsible by means of cross examination, intradermal tests, food diary and elimination diets. When the allergen or allergens have been identified, intensive immunization of the patient should be carried out. Of a group of fifty-two cases of perennial rhinitis 89 per cent were thus identified as allergic in origin. Multiple sensitivity was present in the vast majority of patients but with rare exceptions rhinitis was the sole clinical manifestation. Dust sensitivity predominated over all others in frequency, accounting for 95 per cent of the cases. Sensitivity to occupational allergens other than dust was demonstrated in 41 per cent of the patients, including clothing workers, furriers, bakers and so on. Treatment consisted in active immunization against all specific allergens that could be discovered, or avoidance of them. In some cases the patient had to give up his job.

Allergy of the skin

The pathogenesis of urticaria.—T. Lewis has studied the vascular axon reflex in human skin as exhibited in a case of urticaria. The patient, a woman aged twenty-six, complained of an urticarial eruption which had appeared three months before, two months after her husband (who was in the Army) was posted as missing, and which had continued ever since. Personal or family history of eczema, asthma or hay fever was not obtained. The rash came on when the woman was warm in bed at night, when she was sitting beside the fire or when she was taking a hot bath. On examination the patient was unemotional and did not exhibit signs of any disease. She was kept under observation for a month, on few days of which the skin remained quite clear of eruption. Scattered wheals could usually be found on some part of the body, and during what she called 'attacks' the wheals often became confluent and her face was engorged with blood. The eruption was brought out by a bath at 43° C. but not by one at 38° C., which was chosen as representing the maximum temperature to which her skin could rise when she was in bed. Immersion of the legs only at 45° C. produced a generalized rash. Application of heat, freezing, severe pressure or faradism to small areas of skin caused unusually pronounced hyperaemia of the area itself, with redness and the appearance of a crop of wheals on a surrounding zone of skin extending up to six centimetres beyond the stimulated area. The wheals began to appear from four to eight minutes after the stimulus was applied and continued to appear for about twenty minutes. The experiment was tried of placing a drop of 1 in 300 solution of histamine on the skin and of pricking through it. A similar constellation of urticarial wheals appeared, in addition to the normal urticarial reaction at the site of the prick. The reaction was shown to depend upon the integrity of the cutaneous nerves, being abolished by local anaesthesia. Moreover an area of the skin thus rendered anaesthetic failed to participate in the reaction produced by stimulating a contiguous area. Block anaesthesia failed to abolish the reaction, which is thus proved to be independent of the central nervous system. Flare and satellite wheals are regarded as being produced by the same nervous mechanism, the axon reflex, which causes release of histamine in the affected area. Evidence has been adduced that cholinergic nerves are concerned, and that they constitute a special 'nocifensor' system, distinct from the sensory nerves of the skin. The peculiar sensitivity of the patient's skin was thought to be related to some abnormal constituent of the blood, her serum when injected intradermally producing unusually severe skin reactions in several normal subjects.

Hay fever

Clinical picture and diagnosis.—D. Harley defines hay fever as a type of paroxysmal rhinitis due to hypersensitivity to the pollen of the grasses, which in susceptible people produces symptoms when it comes in contact with the mucous membrane of the upper respiratory passages and eyes. This normally takes place only during the pollinating season of the grasses, which in England begins about the third week in May and lasts until the middle of July. At other times of the year symptoms are absent but can be artificially evoked by applying dried pollen or pollen extract to the mucous membranes, they consist of irritation and swelling of the mucous membrane of the nose and attacks of sneezing with profuse serous discharge, which leave the patient quite exhausted. Itching of the eyes, congestion of the conjunctivae and lacrimation occur. Asthmatic symptoms are often present, especially towards the end of the pollen season, and tend to become worse with each successive year. The intensity of the symptoms varies with the weather and the locality, depending upon the concentration of pollen in the air. This is reduced in wet weather or in closed rooms, but pollen, being very

light, is carried by the wind for such long distances that it is practically ubiquitous. The term, hay fever, should be reserved for the allergic reaction produced by grass pollens and should not be applied to the similar but non-seasonal syndrome resulting from sensitivity to animal dandruffs, orris-root and other substances. Nor should it be used to designate the seasonal allergic rhinitis occasionally caused by tree, weed and flower pollens, such as the type caused by the ragweeds which occurs in America and is better termed ragweed fever. In Great Britain the autumn *Compositae*, especially the Michaelmas daisies, and heather are the commonest offenders. The incidence of hay fever appears to be about the same in both sexes, with possibly a slight preponderance in males. In two different series of cases the ratio of males to females was 52 : 48 and 48 : 52 respectively. In a group of 200 patients the incidence was highest in the decade eleven to twenty years, and fell to almost nil by the age of fifty-one; 63 per cent of the patients were under twenty-one years of age. Most of the older data show a higher incidence at more advanced ages. The author suggests that modern diagnostic facilities have removed many younger cases from the category of 'summer cold' to that of hay fever. Heredity appears to be an important predisposing factor, but opinions differ as to whether the type of inheritance is dominant or recessive. The character inherited is the general allergic disposition, not necessarily the particular clinical manifestation of this. The differential diagnosis of hay fever requires the exclusion of the common cold, chronic infective nasal catarrh and sinusitis, vernal conjunctivitis and allergic rhinitis due to other antigens. The characteristic symptoms and periodicity usually render diagnosis easy, and it is confirmed by producing a skin reaction with grass pollen extract. The test is best carried out by placing a drop of pollen extract on the skin and pricking the skin through it with a needle. When the reaction is positive, wheal formation with surrounding erythema takes place within fifteen minutes. A positive reaction to minute quantities (one-millionth of a gramme or less) of dried pollen or the equivalent extract is obtained in almost every hay fever patient. The changes in the skin are similar to those caused by histamine, and it is thought that the reaction is produced by histamine or a similar substance liberated from cells injured by the allergic reaction. It has been much debated whether the skin reacts specifically to different grasses. It appears at least that the grass pollens are immunologically closely similar, if not identical. Skin tests have been carried out on a number of hay fever patients using eight different grass pollens and it has been shown that the resulting reactions varied in severity, but that no patient who reacted to one pollen failed to react to all. Immunization with extracts of three different grasses, separately or in combination, was found to abolish the skin reaction not only to that pollen or combination of pollens but to all the other pollens also. For routine testing it is enough to use timothy pollen extract only.

Skin testing in children.—According to A. V. Stoesser, hay fever in children is apt to be neglected. He analysed the figures obtained at a paediatric out-patients' clinic and found that symptoms of hay fever were present in about 20 per cent of the patients brought to the clinic because of allergic disease. The condition was commoner in boys than in girls and had usually started quite early in life; a few patients showed symptoms during their first year, many more during the second year, and the numbers rapidly increased during the pre-school period. Most of the children, however, had begun school before being brought for treatment. The attacks had usually increased in severity during school life and the child had thus come to attract medical attention. Skin tests were carried out on all children (413) attending the clinic for hay fever during the period 1936 to 1941. The 'pressure-puncture' method of testing was used—a drop of decinormal sodium hydroxide was placed on the cleansed skin of the forearm and a small amount of dried pollen mixture was stirred into the drop with a tooth-pick, after which from two to four punctures were made through the drop. Sixteen groups of pollens were used for testing, including the grasses and various trees and weeds. A few of the patients gave a negative reaction. The majority of these had had symptoms for only one year, and in some cases a positive reaction was obtained after injection of the child's own serum into his skin, indicating that skin sensitivity had not yet developed in the natural way. Many of the younger children showed relatively small cutaneous reactions, but larger than the control; these were counted as positive. Some patients gave much more pronounced reactions to the tree and grass pollens than to the weeds; some of these children had symptoms only during the season when ragweed pollinates. The *Compositae* mixtures occasionally produced a very large reaction which engulfed the adjacent ragweed pollen reaction; in these cases the children were found to respond well to treatment with an extract containing little *Compositae* pollen and much ragweed. Some weak reactors to grass pollen required specific treatment with grass pollen extract. The best results from skin testing were obtained during the winter months. Ragweed pollen gave the largest number of positive reactions (306). Grass pollen reactions were observed in seventy-two children (17.4 per cent). Specific pollen therapy was undertaken in 310 children. The extracts were freshly prepared for each patient. Prolonged pre-seasonal treatment, consisting of from twenty-five to thirty-five injections started in the late winter or early spring, gave very satisfactory results. Perennial treatment was equally satisfactory. Oral administration of the pollen was tried, but the results of this were not encouraging. Of various non-specific remedies only potassium chloride appeared to be of some benefit; it was given in doses of 5 grains three times a day after meals during the pollen season to children coming too late for specific therapy, and the results were considered sufficiently good to warrant further trial.

Treatment by pollen extracts in oil.—S. J. Taub and E. Rubens present a report on the use of pollen extracts in oil in the treatment of hay fever. The advantages of oily solutions are the slowness with which absorption takes place and the higher concentration that can be attained. Hence a single large dose can be given without risk; with aqueous extracts the rapid absorption of the active principle may result, in a sensitive patient, in severe local and constitutional reactions. Since dry pollen is almost insoluble in any oil, the oily extract was prepared by freezing an aqueous 3 per cent pollen extract in a carbon dioxide and carbon tetrachloride mixture and evaporating it to dryness *in vacuo*, the residue being dissolved in sterile sesame oil. The latter was chosen because not one case of sensitiveness to it has been reported. Solution in sesame oil takes place so slowly that it was found necessary, in order to prepare a 20 per cent solution, to leave the residue in contact with the solvent for six days at room temperature. The sterility of the oily solution was assured by incubating cultures from it for seven days at 37° C. It can be kept indefinitely at room temperature without deterioration. The presence of the active principle, unaltered by the freezing process, in the oily extract was demonstrated by intradermal tests carried out in 200 sensitive patients. Delayed positive reactions were obtained in all of them. Control tests with sesame oil were negative. The erythema and itching came on about thirty minutes after the intradermal injection and persisted for about an hour, in a few patients for considerably longer (twenty-four hours). A week's quiescent interval was followed by the reappearance of a local raised red itching papule, showing that absorption was still going on. There was not any case of constitutional or severe local reaction.

Use of pollen antigen hydrochloride.—The advantages of pollen antigen hydrochloride over the crude extract for treating hay fever are, according to G. E. Rockwell, as follows. (1) It can be more accurately standardized. (2) It is relatively insoluble and is therefore more slowly absorbed and less likely to give general reactions, and the dosage can therefore be higher and more rapidly increased. (3) Because of the higher dosage it gives greater desensitization. (4) It can be used for highly sensitive subjects who are difficult to treat with the crude extract. (5) It keeps much better. The author has treated patients for several years with pollen antigen hydrochloride; for the pollen season of 1941 his statistics show that seventy patients were treated, of whom sixty-two had attacks in the autumn and were ragweed sensitive, whereas eight had spring attacks and were sensitive to various grasses. Of the cases of autumn type, fifty of the patients were treated pre-seasonally, four perennially and eight co-seasonally. All the spring type patients were treated pre-seasonally. The results were very good, being classed as unsatisfactory (less than 75 per cent relief) in only three of the cases—all ragweed-sensitive individuals. The eight ragweed-sensitive subjects treated co-seasonally are not included, owing to the difficulty of estimating results in them. The maintenance dose for the ragweed-sensitive patients, excluding again the eight treated co-seasonally, varied from less than 12,000 units to 30,000 units, the average being 12,000 units. The average number of doses was less than one-half the average number required by patients treated with the crude extract. Patients who were carried up to a maintenance dose of 21,000 units or more showed great diminution or absence of skin reaction to pollen antigen hydrochloride at the end of the course of treatment. Reactions were fewer in number and much milder than those observed in patients treated with crude extracts; only one really severe reaction was noted.

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ALOPECIA

See also B.E.M.P., Vol. I, p. 337.

Regional and diffuse alopecia

Acquired alopecia

Total alopecia with ocular changes.—A case of total alopecia associated with ocular disorders is reported by J. E. Pisetsky and P. J. Kozinn. The patient, a girl aged ten, complained of falling out of the hair, which had begun at the age of two and a half years, and which was not preceded by an illness of any kind. Within a period of two months she had lost all her hair, eyebrows and eyelashes. On examination the child's body was almost completely devoid of hair. Ocular changes were also present and consisted in atrophy of the temporal side of the left optic disk with 'blue-green accumulation' around the macula; associated with the above appearances were a central scotoma and a diminution of the nasal field. Left internal strabismus was also present. Although the patient's father was syphilitic, the child's Wassermann reaction was negative, both in the blood and in the cerebrospinal fluid. The girl wore a wig which was found to harbour pediculi; she had also pediculosis corporis. Treatment of the pediculosis and general ultra-violet therapy were given but lasting improvement did not take

place. No cause for the condition could be discovered, but it was ascertained that a brother of the patient had suffered from temporary patchy alopecia when he was a child.

Calvities

Aetiology and the male hormone.—J. B. Hamilton of the Department of Anatomy, Yale University, states that 'male hormone stimulation is prerequisite and an incitant in common baldness' and points out that there are reasons, such as the onset of alopecia after the assumption of sexual maturity and the preponderant occurrence of common baldness in males (43 per cent in males, 8 per cent in females), for the suggestion that an endocrine factor may be of importance. He has investigated 104 eunuchs and eunuchoids (persons showing a condition in which the testes are present but do not have a normal endocrine function). These subjects of testicular insufficiency included (a) twenty men in whom the deficiency occurred prepubertally, ten of whom were eunuchoids between the ages of twenty and sixty-nine years, and ten were men who were castrated when eight to twelve years old and now are between nineteen and fifty-six years old; (b) thirty-four men who were castrated during adolescence, that is between fourteen and nineteen years old and are now twenty-one to fifty-seven years old; and (c) fifty men who were castrated after achieving sexual maturity between the twentieth and forty-third years of age, and are now between thirty and sixty-one years of age. The author presents evidence that male hormone substances (androgens) are an inciting factor to alopecia and that both their action and a genetic predisposition are prerequisite to the development of alopecia.

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ALZHEIMER'S DISEASE

See also B.E.M.P., Vol. I, p. 354.

Clinical picture

Terminal stages

Clinical picture and morbid anatomy.—A case of the presenile psychosis known as Alzheimer's disease is reported by A. P. Bay and J. Weinberg. The patient, a woman aged fifty-two, began to show signs of mental change four years before her death. The symptoms were loss of memory, difficulty in expressing herself, depression and inability to manage her house. X-ray examination showed a somewhat small skull with a thickened vault, slight pineal calcification and a small normally shaped sella turcica. Encephalography showed dilatation of both lateral ventricles and increased sulcar space in the temporal and frontal areas. Three months before death neurological abnormalities were found as follows: sustained horizontal nystagmus to the right, slight left facial weakness, increased tendon reflexes and Babinski sign on the right side, absence of abdominal reflexes, coarse tremors of hands and tongue and motor aphasia. Laboratory tests gave negative results. The patient became progressively worse, was unsteady on her feet and very irritable, crying out frequently. She died in hospital and a necropsy was performed. The findings in regard to the brain were: weight without dura mater 760 grammes, frontal gyri somewhat atrophic, basal vessels moderately thickened but not unduly so for the patient's age. Serial sections showed slight symmetrical dilatation of the ventricles. Microscopically the cellular content of the cortex was much reduced, in some areas to one-third of the normal, and the cells showed various abnormalities of structure. Numerous intercellular masses of argentophil material were observed. The cerebrum showed gliosis, slight in the cortex, more pronounced in the white matter.

Bay, A. P., and Weinberg, J. (1942) *J. nerv. ment. Dis.*, **96**, 378.

ANAEMIA

See also B.E.M.P., Vol. I, p. 408; and Cumulative Supplement, Key No. 59.

Pernicious anaemia

Aetiology

Hypopituitarism.—L. J. Witts reports two more cases in support of his hypothesis that pernicious anaemia is due to a hormonal element which can produce degeneration of the cells secreting the intrinsic factor. The incidence of pernicious anaemia increases with age, and its association with hypopituitarism may be considered as an example of the precocious senile changes to which patients with pituitary gland disease are prone. Conversely, some of the symptoms of pituitary gland disease may be due in rare instances to associated pernicious anaemia and may be amenable to liver treatment. Of the two patients described, the first, a man aged fifty-eight, developed bitemporal hemianopia and pernicious anaemia at the age of fifty-six. He had one undescended testicle, he had not married until he was forty-six and had not any children. X-ray examination showed an enormous pituitary fossa with intrasellar calcification, and a diagnosis of craniopharyngioma was made. The anaemic condition was improved by liver treatment. The second patient, a small wizened woman of forty-four, had never menstruated and the genitalia and breasts were underdeveloped. The pituitary fossa was small. The excretion of 17-ketosteroids was less than 3 milligrams a day. Atrophy or functional deficiency of the anterior lobe of the pituitary gland was diagnosed. She had signs of typical Addisonian anaemia which was successfully treated by administration of liver extract.

Pathology

Histological observations.—J. P. McGowan regards pernicious anaemia as a condition of unknown aetiology resulting from perversion of erythropoiesis. It is characterized by the appearance in the circulating blood of the megalocyte, or primitive erythrocyte. The red bone marrow, which is greatly increased in amount, shows extreme activity but, possibly because this leads to circulatory congestion, fewer erythrocytes are delivered into the circulation. The megalocytes appear to be abnormally prone to undergo haemolysis in the blood stream, so that excess of bilirubin is found in the blood and haemosiderosis is present in various organs. Anisocytosis with increased coefficient of variation is observed, and microcytes and poikilocytes as well as megalocytes are found in the blood. The colour index is of comparatively little diagnostic importance. Anti-anaemic factor (liver) produces great improvement in the blood but apparently cannot restore normality, the coefficient of variation, for example, remaining high. The changes in the bone marrow appear to be irreparable and progressive, and the disease can only be retarded, not cured, by continuous administration of anti-anaemic factor. Refractory cases, on this assumption, are those in which there is a peculiarly intractable type of marrow lesion. Subacute combined degeneration is an increasingly common complication, owing to the prolongation of life by liver treatment; it may occur before pernicious anaemia is diagnosed. In pernicious anaemia the erythrocytes do not form rouleaux, and the author thinks that anoxia of the cord may result from the absence of the distending effect which is produced by rouleau formation in the capillaries. He is further of the opinion that achylia is merely coincidental.

Clinical picture

Incidence of carcinoma of the stomach.—P. C. Doehring and G. B. Eusterman draw attention to the comparatively common occurrence of carcinoma of the stomach as a complication of pernicious anaemia. With the introduction of liver therapy the expectation of life in patients with pernicious anaemia was considerably increased and, as might be expected, the incidence of gastric carcinoma appears to have increased with the longer survival period. During the five years 1935-9, 1,014 people were treated at the Mayo Clinic for pernicious anaemia. Of this number seventeen subjects (1.7 per cent) also had carcinoma of the stomach. In 1938, in the United States of America, 23,666 persons over forty years of age died of gastric or duodenal carcinoma, this number represents a death rate of 0.57 per thousand for this disease. On the assumption that carcinoma of the stomach exists for five years before causing death, the incidence in the group in question becomes 2.85 per thousand, even if ten years be taken as the average duration of the disease, the mortality rate is still less than 6 per thousand. Hence an incidence of 17 per thousand would be distinctly higher than would be expected if the number of persons with pernicious anaemia was comparable with the number of ordinary persons in the general population over forty years old. Pernicious anaemia is rarely seen under the age of thirty. In all but two of the authors' seventeen cases it was thought that pernicious anaemia had preceded the onset of carcinoma by from two to fifteen years, although the insidious development of carcinoma makes this point difficult to establish. In the other two cases both diseases were present at the time of the first examination and it was impossible to say which had started first. The average age at onset of pernicious anaemia was 54.5 and of carcinoma 63.2 years. No difference was noted in the situation of the growth or in the grade of malignancy between uncomplicated cancer of the stomach and cancer complicating pernicious anaemia. Achlorhydria is common to both conditions but should be regarded as a symptom rather than as a clinical entity, moreover, it is common among people over middle age not suffering from either disease; it has been estimated to occur in 40 per cent of people over sixty. It is far too common to be regarded as the direct cause of either pernicious anaemia or carcinoma of the stomach. Achlorhydria is not the result of gastritis in every instance, but chronic gastritis is a common concomitant both of pernicious anaemia and of gastric cancer.

Megalocytic anaemia and pregnancy*Megalocytic anaemia of pregnancy*

Incidence, symptoms and treatment.—A series of twenty-three cases of pernicious anaemia of pregnancy is reviewed by H. G. Miller and T. C. Studdert. In few of the patients was the disease suspected by the doctor and many of the patients were left to become dangerously ill before investigation and treatment were carried out. The patients' ages ranged from twenty-two to forty-one years; eighteen women were less than thirty-five years old, although during the same period 222 women with pernicious anaemia were admitted to the hospital, of whom only twelve were under thirty-five years of age. Of the twenty-three patients twenty were delivered of healthy babies, two gave birth to still-born infants and one had twins. In one case only the child showed iron-deficiency anaemia (haemoglobin 64 per cent, colour index 0.73). All the patients when first seen were already in the puerperium; the onset of symptoms had generally occurred after the seventh month of pregnancy. The chief complaints were pallor, tiredness and shortness of breath. Thirteen women complained of sore tongue, and five of paraesthesia. Pyrexia was common; during treatment the fever on an average lasted ten days. Retinal haemorrhage was present in ten of twenty-one patients examined ophthalmoscopically. Vibration sense and deep reflexes were normal. Glossitis was present in two cases; in most patients the tongue was pale, with atrophied papillae. Three patients had histamine-refractory achlorhydria, seven had hypochlorhydria, eleven had normal hydrochloric acid. The

erythrocyte count was below 500,000 in one case; between 500,000 and 1,000,000 in eleven cases; from 1,000,000 to 3,000,000 in the rest. Sternal puncture confirmed the diagnosis in six cases. All the patients responded to specific treatment, which was afterwards discontinued in fourteen. For the patients with free hydrochloric acid a good diet including Marmite usually proved sufficient. If achlorhydria was present or Marmite therapy failed, liver extract was given parenterally or by mouth. Iron deficiency necessitated treatment in some cases.

Recognition and treatment.—Sixteen cases of megaloblastic anaemia complicating pregnancy and the puerperium have been studied by L. S. P. Davidson, L. J. Davis and J. Innes. Half the patients were primigravidae or primiparae; twelve were seen either before any liver treatment had been given or within a week of its being started; none had been having it for more than two months. Only two were over forty years old and the average age was 30.8, which is considerably lower than the ages commonly met with in Addisonian pernicious anaemia. In further contrast to the latter, the colour index was within or below normal limits in ten of the patients, and macrocytosis was present in only nine. Sternal puncture was performed in thirteen cases, and twelve films showed numerous megaloblasts. Of fourteen patients tested for achlorhydria, only four showed a positive reaction. All the patients were treated by being given liver extract injections; five responded satisfactorily within a week. Ten patients were refractory to treatment for periods varying from eleven days to several months; in each case several brands of liver preparations were tried, and iron was given. Many also received yeast and ascorbic acid. In twelve patients, blood transfusions were used to sustain life. In six of the refractory cases sepsis may have played a part in the patients' delayed response to liver therapy. Stress is laid upon the importance of early recognition and adequate treatment, to guard against the danger of the acute exacerbations which may occur during the last two months of pregnancy and the disastrous fall in the blood count which may result from the normal blood loss during labour.

Macrocytic hyperchromic anaemia of pregnancy

Clinical picture.—M. Daniel and M. Antus report a case of macrocytic hyperchromic anaemia of pregnancy, which they describe as a rare condition believed to be the result of a deficiency of the erythrocyte maturing factor. The case was the first recognized in a series of 18,000 deliveries. The disease is uncommon in temperate climates, but is prevalent in India where dietetic deficiencies are particularly common. Macrocytic anaemia may recur in successive pregnancies and may become progressively more severe. The mortality among untreated patients sometimes reaches 90 per cent. Grave symptoms may develop suddenly just before, during or after delivery. The writers' patient, a woman aged twenty-nine who had already had two children and three miscarriages, was admitted to hospital at term complaining of increasing pallor, weakness and shortness of breath on exertion. Blood examination showed: haemoglobin 18 per cent, erythrocytes 850,000, haematocrit reading 12 per cent, total serum protein 4.9. The urine contained albumin and casts. No signs of external or concealed haemorrhage could be detected. The patient was immediately given a transfusion and received 1,400 cubic centimetres of citrated blood during a period of fourteen hours, her general condition was then greatly improved and blood examination showed haemoglobin 33 per cent, erythrocytes 2,100,000, haematocrit 18 per cent, colour index 0.8. A more detailed examination of the erythrocytes showed many macrocytes, moderate anisocytosis and poikilocytosis, occasional polychromasia, with 0.2 per cent of reticulocytes. It was found that on account of severe vomiting the patient had been subsisting entirely on two glasses of milk and water a day for the two months previous to examination. Analysis of the gastric contents was made and sternal puncture was performed. The former investigation gave normal results, but the results of the latter confirmed the diagnosis of macrocytic anaemia of pregnancy. When treated by a high vitamin B diet and by parenteral liver extract, the woman recovered rapidly.

Hypochromic deficiency anaemias

Idiopathic hypochromic anaemia

Diet and haemoglobin.—In a Discussion by the Section for the Study of Disease in Children of the Royal Society of Medicine, the war-time problem presented by nutritional anaemia in children and women was dealt with from various aspects. Helen M. M. Mackay, Lucy Wills, R. H. Dobbs and Lady Bingham discussed the influence of economic status and of diet on the mean haemoglobin level. Although no generally accepted standards of haemoglobin level have been fixed, it has been shown, for example, that in pregnant women a steady fall from an average of 90 per cent haemoglobin is seen for those with an income of from 25s. to 40s. per head after payment of rent to an average of 76 per cent for those with under 6s. per week. Few data are available for children of different economic status, but such figures as have been published show a similar drop in haemoglobin levels in the poorer subjects. Anaemia in babies appears to result, in part at least, from anaemia in their mothers during pregnancy. Moderate degrees of anaemia exert a considerable effect upon health in children. In working-class families babies who had received iron were found, at the age of one year, to have a mean haemoglobin level 13 per cent higher than that of controls, to weigh more and to have approximately half the morbidity rate. It is probable that in war-time the mean haemoglobin level of school children varies with the food available. Various groups of women examined since the present war began all showed haemoglobin levels significantly below pre-war figures obtained by other workers. Every effort should be made to ensure the best

possible diet for pregnant and nursing women and for growing children and, since war-time diets are likely to be deficient in iron, it is probably advisable to institute iron prophylaxis or treatment as well. L. Findlay, before the war, failed to discover any serious incidence of anaemia in London children attending hospital for various ailments. The results were the same whether the blood was obtained from the ear or from the finger or heel. Since war broke out considerably lower average figures have been obtained in Oxford children who appeared otherwise healthy and well grown, that is who did not show any evidence of defective feeding. A high haemoglobin level is not necessarily a sign of good health; lower values may be related to more salubrious surroundings and more available oxygen. Iron in large doses exerts little or no influence on the haemoglobin level of a normal child. R. H. Dobbs discussed the difficulty of obtaining accurate haemoglobin readings and stressed the importance of obtaining freely flowing blood from a warm limb.

Chlorosis

Need for certain minerals in the diet.—In a Leading Article entitled 'Is anaemia prevalent?' the *British Medical Journal* points out that higher standards of accuracy are now demanded of workers in this field. The haemoglobinometer must be standardized in terms of oxygen capacity or N.P.L. specification. Venous blood should be employed and it is advantageous to estimate not only the size and haemoglobin saturation of the red cells but also the serum albumin and the vitamin C content of the plasma or of the white cell layer. It is better to avoid the word anaemia and to use statistical language in presenting results. Recent investigations upon women and children have shown that women working in factories have a higher mean haemoglobin level (94 per cent) than nurses and students of the same age (90.6 per cent), whose haemoglobin level again is higher than that of nurses and students working in sector hospitals in the country (84.1 per cent). A fall appears to have undoubtedly taken place among nurses and women students since 1931, when the mean haemoglobin value was 98.3. The 'country' group was found to be receiving a daily diet of only 1,662 calories, 47 grammes of protein and 9 milligrams of iron. One in every eight nurses who went out to the sector developed clinical anaemia in six months. This and other recent work suggests that too much attention has been paid to the iron content of the diet and that the importance of other constituents (calcium, phosphorus and protein) has been overlooked. Official action has been demanded, but it is foolish to ask for extra rations or government action when people who should know better are not making the best use of the food available. If the woman factory hand can procure a proper diet it ought to be possible for students and nurses to do so.

Haemolytic anaemias

Sickle cell anaemia

Aetiology, the sicklaemic trait.—M. A. Ogden records two fresh cases in two new white families—in a girl aged nine years and in a boy aged eight years. The girl was of Spanish descent, the boy of German, negro and mixed Indian and Scottish extraction. From examination of previously reported cases Ogden classified six as active sickle cell anaemia and twelve cases of sicklaemia. The problem of whether these conditions are confined to the negro race or whether they may occur in members of white and yellow races without admixture of negro blood is not yet satisfactorily solved. The author believes that a sickle cell trait or sicklaemia is definite evidence of negro blood and argues that sickle cell anaemia is a national public health problem, especially in the United States. Inter-marriage between whites and negroes directly endangers the white race by transmission of the sicklaemic trait.

A case record.—J. Stasney records a case, with necropsy, in a negro boy, fourteen years of age, with sickle cell disease and abnormal destruction of the red blood cells and haemosiderosis in the liver and spleen. Three years before death the patient had had rheumatic fever followed by mitral stenosis. The spleen (24 grammes) was firm, fibrotic, small and purplish in colour. The liver (3.6 grammes) was much enlarged, with distension of its sinusoids by red blood cells and sickle cells in the sinusoids; Kupfer's cells showed great over-activity whereas the splenic reticulo-endothelium appeared to be inactive. A large proportion of the red blood cells in all the organs, especially the hepatic sinusoids, were sickle-shaped. The size of the spleen was chiefly seen to be enlarged in early life, whereas a small atrophied spleen was characteristic of the later stages. Twelve cases of sickle cell disease, from 4,094 necropsies, were studied; these were divided into (a) those with large or normal sized spleens and (b) those with sidero-fibrotic spleens and enlarged livers.

Acute or subacute haemolytic anaemia (Lederer)

Differential diagnosis in pregnancy.—F. G. Lescher reports on seventeen cases of severe anaemia associated with pregnancy. Nine were of the pernicious and eight were of the haemolytic (Lederer) type. All the patients in the first group were multiparae and their ages ranged from twenty-seven to thirty-seven years, averaging thirty-one years. Two gave a history of very distressing vomiting during pregnancy. In six cases the onset of the anaemia was insidious with increasing pallor, weakness and breathlessness; in three patients symptoms developed suddenly soon after delivery. Pyrexia occurred in several cases. The blood changes resembled those seen in Addisonian anaemia. The gastric juice contained a normal amount of hydrochloric acid in only two cases; in two it was absent and in five diminished. In three cases the hydrochloric acid content rose to a normal level after delivery. All the patients responded well to specific treatment, and have remained well for as long as they have been observed subsequently, that is for from one year to eight years. Of the patients with haemolytic anaemia

one died; the others were successfully treated by blood transfusions. The chief differentiating point between the haemolytic type and the pernicious type of anaemia is the strongly positive indirect van den Bergh reaction observed in the former condition. Haemolytic anaemia, moreover, does not respond to liver therapy.

Refractory haemolytic anaemia.—J. C. Sharpe and J. P. Tollman record and discuss five cases, three with necropsies, in which they were unable to influence the clinical course of haemolytic anaemia by conservative medical treatment with blood transfusion, iron or liver or by splenectomy, which was performed in all the cases. The patients, two males and three females, were all adults; their ages ranged from twenty-five to sixty-two years, four of the five being between fifty-eight and sixty-two. There was not any evidence of congenital haemolytic jaundice, but some American writers have regarded such cases as being the acquired form (Hayen-Widal) of haemolytic jaundice or as atypical haemolytic anaemia. The classification of the haemolytic anaemias has been vague and ill defined and no attempt is made to provide a satisfactory classification by the authors, whose five patients presented various degrees of pallor, jaundice and impaired nutrition. The jaundice was moderately severe. In three cases the erythrocyte count was one million, or slightly less, per cubic millimetre. The erythrocytes were of the macrocytic type in three cases; stained blood smears failed to show the spherocytes which are so characteristic of familial haemolytic jaundice. The mean corpuscular haemoglobin concentration was 31 per cent. In four cases reticulosis was a striking feature. The leucocyte count ranged from 1,400 to 4,000 per cubic millimetre. In all five cases cholecystograms showed the presence of biliary calculi. The spleens were moderately to markedly enlarged; histologically there was striking reticulum-celled hyperplasia. The bone marrow showed advanced erythropoietic activity. In two cases blood transfusions produced dangerous and alarming reactions.

Acholuric jaundice

Report of further research

J. V. Dacie continues the report of work done mainly in 1938 and 1939 on the disease first described in 1907 by A. Chauffard as *l'ictère congénite de l'adulte* and now entitled familial haemolytic anaemia (because the jaundice is secondary to increased haemolysis), in preference to 'familial acholuric jaundice', the name widely used in British but not in Continental and American papers. Acceptance of a case as one of familial haemolytic anaemia is based on the following criteria. Anaemia of the haemolytic type with increased susceptibility of the erythrocytes to haemolysis by hypotonic saline, spherocytosis, an abnormal tendency of the blood to undergo haemolysis *in vitro* on incubation at 37° C., and splenomegaly, in which engorgement with blood is the outstanding feature. A history of recurrent anaemia or jaundice over a period of years and a positive family history is taken as confirmatory, although not essential, in diagnosis. In twenty-four patients quantitative estimation was made of the erythrocyte fragility by the method used by Creed and modified by Dacie and J. Vaughan. The fragility of the red cells before splenectomy, though variable in form, was classified into three main types on the basis of their shapes, 'tailed', 'diagonal' and 'normal'. Splenectomy was performed on twelve patients, in eleven of whom resistance to haemolysis was increased after the operation. The histopathology of the spleen in the twelve cases shows great engorgement with blood as the most notable change; perfusion experiments with excised spleens failed to demonstrate the cause of the congestion. Although it was difficult to free the pulp from the blood by perfusion with saline, the time of circulation of test objects (fowl erythrocytes) through the spleen appeared to be normal. The available evidence suggests a haemolytic disorder, based upon the presence of erythrocytes with an increased tendency to haemolysis; but although there is much to support the view that this represents a primary defect in erythropoiesis, experimental and clinical observations on the relationship between haemolytic anaemia, splenic congestion, and spherocytosis indicate that the possibility of the presence of an abnormal haemolytic agent or metabolite cannot be ignored.

EDITORIAL COMMENTARY—Anaemia and the Present Time

Recently, attention has been redirected by several groups of workers to the common occurrence of anaemia in children and in women, particularly during pregnancy and the puerperium, confirming earlier observations. The commonest anaemia of pregnancy is well known to be the nutritional iron-deficiency hypochromic microcytic anaemia, in which patients usually respond so well to adequate iron therapy (for example ferrous sulphate, 9 grains taken three times a day), and which may or may not be associated with achlorhydria gastrica. The anaemia usually develops during pregnancy and becomes increasingly severe, but may only manifest itself in the last few weeks of pregnancy or during the puerperium. It is now clear that, under war-time conditions of food rationing, other factors have arisen, because very many patients may show variable degrees of vitamin C deficiency—sometimes even frank scurvy—and an inadequate supply of first-class protein also appears to play a part in causing such a type of anaemia. Consequently, for satisfactory treatment vitamin C and some first-class proteins should be added to the patient's diet. Much less often anaemia of pregnancy is of the megalocytic or megaloblastic type, and more of these types of case have been reported since I dealt with the subject in 1932. They fall into three main groups. (1) Patients with true pernicious anaemia who are pregnant, or who first show positive signs of pernicious anaemia under the strain of pregnancy; (2) patients with the so-called megalocytic or 'haemolytic'

anaemia of pregnancy; (3) patients with the tropical megalocytic anaemias. Patients in the first group are treated in precisely the same way as, and respond exactly like, patients with pernicious anaemia, and they must continue treatment for life. Patients in the second group recover completely after similar treatment but in an occasional refractory case preliminary blood transfusion may be required. In the third group, those with tropical anaemias, as confirmed recently by H. C. Trowell, 1943, may have a mixed form ('dimorphic anaemia') showing deficiency of iron and of the anti-pernicious anaemia principle. Here again, deficiencies of vitamin C and of first-class protein (or extrinsic factor) are important contributory factors which should be rectified during treatment. I have drawn attention (1942) to these points several times lately, because it has become increasingly obvious in my clinics, while the war has progressed, that patients with previously well controlled and stabilized chronic anaemias, such as pernicious anaemia, are failing to maintain their improvement and normal blood count, in spite of receiving what was supposedly an adequate amount of liver extract, known to be clinically active. Investigations showed that these slowly failing patients, as well as many patients referred to me with purpuric manifestations, were really scorbutic and that they responded to adequate doses of ascorbic acid. These observations did not explain, however, all the failing cases, particularly of those patients with pernicious anaemia that tended to slip back on previously adequate doses of parenteral liver extracts; it was found that they responded to treatment by pepsac (desiccated hogs' stomach) in doses of 30 grammes daily, making it clear that the extra daily increase of nearly 1 ounce of protein played a very important part in recovery. Similar observations were also made in cases of megalocytic hyperchromic anaemia, resembling pernicious anaemia but without achlorhydria, that have been described as occurring after a deficient intake of the extrinsic factor, which is usually found in meat; consequently treatment by administration of desiccated hogs' stomach is the ideal treatment in such cases, and liver extracts are of less use.

Thus it is obvious that the best treatment in pernicious anaemia and in similar anaemias, under the present conditions of food control, is to give 1 ounce (30 grammes) of desiccated hogs' stomach orally in about three divided doses per day after meals, reducing the dose later when the blood picture returns to normal, by using hogs' stomach for the permanent maintenance treatment not only is haemopoietin, the anti-pernicious anaemia factor, supplied but also extra first-class protein and digestive enzymes such as pepsin, and so forth. Administration of hogs' stomach is still the best treatment for patients with spinal cord involvement. On the other hand, the parenteral use of liver extracts is most valuable in the early stages of severe anaemia or as an adjunct to stomach therapy; when necessary vitamin C should also be given. Undoubtedly treatment of pernicious anaemia in war-time requires more careful supervision and control than previously. In this connexion it is important to realize that, when a previously well stabilized and symptom-free patient with pernicious anaemia begins to complain of vague pains or discomfort, of headaches or of loss of weight without showing blood changes sufficient to explain them, some other complications may be developing. The most important ones to bear in mind and also to exclude are diabetes mellitus, hyperpiesia and malignant disease, which begin very insidiously, the patient indeed may not complain of symptoms until too late. These complications I have considered previously (1933¹; 1933²), while more recently Doebring and Eusterman (1942) have confirmed the slightly higher incidence of gastric carcinoma in cases of pernicious anaemia. Although hypopiesia is almost invariable in the severely anaemic stages of pernicious anaemia, hyperpiesia often develops in the older patients after years of good health, but this does not indicate that there should be a discontinuance of the anti-anaemic treatment which is controlled solely by considerations of the state of the blood count. Diabetes mellitus is not a surprising complication since both conditions are familial in character, and pernicious anaemia is always, and diabetes mellitus is usually, associated with achlorhydria gastrica. There is no difficulty in treating patients with the combined conditions according to their individual needs.

Attention must be drawn to an important problem that has arisen in connexion with aplasia of the bone marrow constituents leading to aplastic anaemia, to agranulocytosis, or to thrombocytopenic purpura. These conditions often occur after exposure to toxic substances such as gold, lead, arsenic, bismuth, chlorinated hydrocarbon solvents, trinitrotoluene and especially the sulphonamide derivatives. During recent years there has been an enormous increase in the use of the sulphonamide drugs which, through improper and unrestricted use, have caused large numbers of fatalities—it cannot be emphasized too strongly that they are very dangerous and should be used only when positively indicated, under careful haematological control. A further and more difficult problem is that of their use, as also the administration of arsenicals, in venereal diseases clinics, in patients who have already suffered liver damage through working with toxic substances, such as solvents and trinitrotoluene in filling and chemical factories. In such cases it is the clear duty of the practitioner or venereologist in areas in which such factories exist, or when the patient is known to work where such risks exist, and before embarking on an hazardous therapeutic course, to make sure first of all—if necessary by reference to the factory doctor—that the patient has not been affected by the work.—JOHN F. WILKINSON.

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ANAESTHESIA

See also B.F.M.P., Vol. I, p. 472, and Cumulative Supplement, Key No. 60.

Choice of anaesthetic*The nature of the operation*

Anaesthesia in abdominal surgery.—As a Leading Article in the *Lancet* points out, the comparative safety of abdominal surgery nowadays is due mainly to improvements in anaesthesia, and it would be irrational not to apply modern methods in the treatment of abdominal wounds whenever facilities are available. Some authors advocate spinal anaesthesia as being the most suitable method in cases of abdominal wounds, but few, in Great Britain at any rate, would favour its use when shock is present. It is dangerous to assume that the fall of blood pressure associated with spinal anaesthesia does not matter and that it can be checked by suitable treatment. In the unshocked patient such a fall is not accompanied by reduction of the circulating blood volume. In shock, however, the blood volume, and therefore the available oxygen transport, is reduced, and general peripheral vasoconstriction is Nature's way of ensuring that the vital centres obtain priority in the matter of oxygen supply. Dilatation of the peripheral blood vessels by spinal anaesthesia counteracts this physiological response. It is stated that some large vessel is almost always divided in the wounded abdomen, and such a possibility must be constantly borne in mind. To delay operation in the hope that shock will abate is dangerous; until the bleeding is stopped improvement is impossible. In cases of abdominal injury shock is seldom present in the absence of bleeding. Russian surgeons advise early operation under local anaesthesia, even in the presence of shock. Splanchnic block combined with local anaesthesia is another method. One disadvantage of local anaesthetics is that *in vitro* they inhibit the action of sulphonamides, but the rapid absorption of the local anaesthetic probably neutralizes any such effect on sulphonamides applied directly to the wound. Most people in Great Britain, both patients and surgeons, prefer a general anaesthetic, and light general anaesthesia may often be used advantageously to supplement local anaesthesia. For such a purpose the choice lies between ether, cyclopropane, and gas and oxygen. Ether is probably the best and safest substance for general use, especially by the non-expert anaesthetist. In shock, maintained anoxaemia is especially dangerous and in anaemic patients it is often difficult to detect, but in the case of ether anaesthesia it is comparatively easily avoided.

The training of anaesthetists

Anaesthesia and the general practitioner.—A Leading Article in the *British Medical Journal* discusses the impression which seems to be current that the standard of anaesthesia in Great Britain as a whole is unsatisfactory. The feeling appears to have its roots in the minds of whole-time anaesthetists, who are responsible both for the modern advances in their specialty and for the critical attitude towards it which has developed. The writer believes that the causes for dissatisfaction can be traced to the fact that medical education has failed to keep pace with the innovations of the past fifty years, during which surgery and anaesthesia have advanced *pari passu*, each aiding the other. The medical student who is to become a general practitioner should be taught, not how to handle some complicated piece of apparatus, but how to use the mask and bottle with safety and efficiency, how to give nitrous oxide without making the patient blue and how to use the intravenous barbiturates. He should have a thorough working knowledge of anaesthesia for minor operations and be well acquainted with the pitfalls that beset the anaesthetist in the occasional major emergency. As things are, he is often left to pick up the rudiments of the art after he has settled in practice. The immediate problem is how to reconcile the ideals of the specialist anaesthetists with the realities of general practice. All are agreed that the curriculum is overcrowded and that the student has little opportunity to learn the old-fashioned methods which he will be obliged to use. Many students when they qualify have probably never seen chloroform administered; yet chloroform is likely to continue to have its uses in general practice. The general practitioner anaesthetist must recognize his limitations and seek to perfect himself in anaesthesia for minor operations, leaving major ones to the specialist anaesthetist.

Ether anaesthesia*Methods of administration*

A new carbon dioxide absorber.—A new type of carbon dioxide absorber is described by W. W. Mushin. The function of a carbon dioxide absorber in anaesthesia is to absorb carbon dioxide from the patient's expired air in any desired proportion; in this way it is possible either to keep the carbon dioxide in the inspired air at a minimum or to allow it to contain a low concentration of the gas. The circuit arrangement described is intended to be used in conjunction with the Boyle anaesthetic apparatus. The patient expires into the bag through a canister of soda-lime and the gas which he inspires comes from the bag through the soda-lime in the reverse direction; absorption is much more complete when this double phase method is employed. The soda-lime canister is easily removable for changing. The bag is of concertina shape to allow of easy manual compression for the purpose of artificial or controlled respiration. An ether vaporizer is incorporated in the circuit. Both ether and soda-lime can be used in a fractional manner. Two gas entry nipples are placed one on each side: one is for oxygen, the other, with a tap, is for the admission of air. The apparatus has been found to give satisfactory results in practice.

Nitrous oxide*Technique of administration*

Prevention of anoxaemia.—The statement that nitrous oxide with oxygen is the safest anaesthetic agent is criticized by R. B. Gould, who points out that although the mixture can produce unconsciousness it can never produce muscular relaxation unless its use is so abused as to be associated with hypoxia; and even in maintaining unconsciousness suboxygenation is often difficult to avoid. Cyanosis is not an invariable concomitant of anoxaemia in an anaemic patient, and the recognition of anoxaemia in such cases is often very difficult. As a practical guide the rule should be to give non-anaemic patients enough oxygen to keep them pink and with anaemic patients to increase the oxygen above the minimal level. This often necessitates the use of a supplementary agent such as ether, which for the non-expert anaesthetist is the simplest, safest and best. The use of ether to supplement gas and oxygen should not be regarded as evidence of lack of skill on the part of the anaesthetist.

Spinal anaesthesia*Technique*

In pulmonary tuberculosis.—W. Bourne enumerates the following principles to be observed when an individual suffering from pulmonary tuberculosis is to be given an anaesthetic. (1) The anaesthetic used should not damage the lung and should cause the minimum disturbance of metabolism; (2) reflexes should be depressed as little as possible, in order that coughing may not be stopped for too long a period; (3) the method adopted should allow for a sufficient supply of oxygen. Ether has an irritant action on the respiratory passages, all the commonly used general anaesthetics give rise to some disturbances of metabolism and lack of oxygen produces changes in the liver and kidneys. Spinal anaesthesia, preceded by adequate doses of some narcotic and accompanied by continuous intrapharyngeal administration of oxygen and intravenous infusion of glucose-saline, is the author's method of choice. The Etherington-Wilson technique is used, in which nupercaine solution, of specific gravity 1.003 (1 in 1,500), is injected in suitable doses, depending on the operation to be performed, with the patient sitting straight upright; he remains in this position for a number of seconds varying from twenty to sixty, according to the level of anaesthesia required, and is then laid down, the head of the table being tilted slightly downwards. The anaesthetic solution diffuses upwards as long as the upright position is maintained. The drugs advised for premedication are $\frac{1}{4}$ grain (0.016 gramme) of morphine and $\frac{1}{100}$ grain (0.016 gramme) scopolamine given ninety minutes before the operation, and repeated in sixty minutes if the effect is not sufficient. Analeptics are not used as a routine, but a mixture of posterior pituitary extract and ephedrine is given if the blood pressure falls excessively. Four deaths occurred during operation in a series of 291 cases, but two of the patients were already *in extremis*. Recovery after high spinal anaesthesia is better than when a general anaesthetic is given.

Nupercaine administration.—R. S. Verster reports 2,000 cases of nupercaine spinal anaesthesia. This drug is active in extreme dilution, of low toxicity in dilute solution, will stand repeated boiling and is rapidly eliminated. It is precipitated by alkalis and must never be used if the solution is not perfectly clear. The dose used in this series of cases varied from 7 to 11 cubic centimetres according to the level of anaesthesia required. The mortality rate was 0.05 per cent. Complications occurred in 6.6 per cent. They were not specific for nupercaine but were the ordinary complications (headache, meningismus, backache) of spinal anaesthesia in general.

Rectal anaesthesia and basal narcosis*Basal narcosis*

Contra-indications and uses.—Conclusions deduced from their experiences with intravenous anaesthesia in 1,157 cases are stated by H. F. Bishop and F. F. Rudder. Evipan (hexobarbitone) was used in twenty-one cases, and pentothal sodium in 1,136 cases. Intravenous anaesthesia is suitable for many minor operations, for painful dressings and for diagnostic procedures of short duration. It may be used in combination with spinal, local or regional anaesthesia or as a method of induction. The following contra-indications are given. (1) Age

less than fifteen years. (2) Inflammatory conditions about the mouth and throat with potential encroachment on the upper respiratory passages. (3) Reduced vital capacity. (4) Advanced hepatic or renal disease. (5) Severe diabetes mellitus. (6) Shock or anaemia. Adequate pre-medication is essential, preferably by means of a morphine-scopolamine preparation. Pentothal sodium has a stimulatory parasympathetic action, and atropine may be necessary to counteract parasympathetic reactions such as coughing, retching and bradycardia; such phenomena are especially liable to occur in operations upon the eye. Cocainization of the pharynx and larynx facilitates the introduction of an airway. The needle should be introduced into the vein right up to the hub to guard against dislodgement. If the veins are small, preliminary hot packing of the limb is valuable. Respiratory failure may occur after intravenous anaesthesia, necessitating prolonged artificial respiration. Oxygen must always be at hand.

Basal narcotics

Pentothal sodium

Intermittent administration.—A new (intermittent) method of administering pentothal sodium is described by R. L. Soper. The intravenous needle is attached to a glass tube. This is connected by rubber tubing to the tail of a glass Y piece of which the limbs are connected to (1) an ordinary saline-drip apparatus, (2) a syringe containing pentothal sodium solution coloured with indigo-carmin. The syringe bears a hypodermic needle over which is fixed a length of fine tubing, for example a ureteric catheter, long enough to traverse the system and to enter the glass tube attached to the intravenous needle. When empty the syringe can easily be disconnected and replaced by a full one.

Uses and dangers.—A. R. Hunter gives the following indications and contra-indications for pentothal sodium anaesthesia. (1) It is suitable for short operations, providing good initial relaxation and subsequent period of sleep. (2) Combined with gas and oxygen it is next best to cyclopropane for extra-abdominal operations, but for intra-abdominal operations it may not provide sufficient relaxation. (3) It is contra-indicated for operations for cervical cellulitis; anoxaemia from any cause greatly increases the depressant effect of pentothal upon the heart, and the special risks associated with operation in such cases, may be due to partial obstruction of the airway. All general anaesthetics are best avoided in cervical cellulitis. (4) It must not be used as the sole anaesthetic when any possibility exists of foreign material entering the larynx. Pentothal so depresses the respiratory centre that efforts are not made to overcome the obstruction and the anaesthetist may therefore fail to recognize the accident until too late. (5) It is unsafe as the sole anaesthetic for operations involving opening the pleura because the consequent vagal inhibition may initiate a vicious circle of anoxaemia and respiratory depression. Carbon dioxide and oxygen must always be at hand when pentothal sodium is used. Other ill effects which have followed its use are allergic dermatosis and thrombosis of the basilic vein.

Cyclopropane

Technique of administration

Clinical merits and demerits.—H. K. Beecher writes on cyclopropane which has now been in use for ten years and has received a trial sufficient to justify a critical examination of its present status. Cyclopropane is a potent anaesthetic agent, producing its effects in a low concentration in the central nervous system. But the degree of muscular relaxation produced is not always comparable with that procurable with ether at a safe level of anaesthesia. It is possible to give a high proportion, as much as 80 per cent, of oxygen with cyclopropane and yet to maintain satisfactory anaesthesia. This is a much higher proportion than the 10 per cent of oxygen which can be given with nitrous oxide or the 20 per cent given with ethylene. Cyclopropane is only slightly soluble in the blood and can be given in concentrations of from 10 to 35 per cent or more. Hence induction of and recovery from anaesthesia are rapid, and deep anaesthesia is reached quickly. The great speed of action, however, makes for a risk of overdosage in inexperienced or careless hands. Cyclopropane disturbs the carbohydrate metabolism very little and in the rare case of an urgent operation upon an uncontrolled diabetic it is safer than ether. Although less irritating than the latter it has a certain irritant effect upon mucous membranes. Its two great drawbacks are its toxic effect on the heart and its explosibility. Laboratory and electrocardiographic studies have shown that it may produce ventricular extrasystoles which sometimes run on into ventricular fibrillation. Death on the table with only brief warning signs has occurred in a number of cases. It is particularly dangerous in cases of thyrotoxicosis. The risk of a serious explosion due to electrostatic sparks is considerably greater with cyclopropane than with ether. In spite of such dangers the great value of cyclopropane on some occasions renders it deserving of further study by well trained anaesthetists.

General

New apparatus

The Oxford anaesthetic vaporizers.—The Oxford anaesthetic vaporizers, which are described in an Annotation in the *British Medical Journal*, embody the results of researches at the Nuffield Department of Anaesthetics to discover a simple means of administering liquid anaesthetics in known concentrations of vapour. To vaporize a liquid, heat must be supplied. In vaporizer number 1 this is achieved by means of three concentric containers placed one inside the other. The inner one contains ether, the intermediate one a 'reservoir substance',

crystalline calcium chloride, which melts at a suitable temperature (30° C.); the outer one is filled with hot water. The reservoir substance acts as a buffer, taking up heat on any rise of temperature, but releasing it only at the temperature of its melting-point. A thermometer is placed in the intermediate chamber, and a sudden fall of temperature is the signal that the reservoir substance has recrystallized and that fresh hot water must be poured into the outside container. The liquid ether, maintained at a constant temperature of 30° C., furnishes a steady high concentration of ether vapour. Air is drawn in through a valve, and reaches the patient either directly or after passing, wholly or in part, over the ether. Remarkably smooth anaesthesia is obtained. In vaporizer number 2 the vaporized ether is mixed with oxygen and, if desired, with nitrous oxide.

Mortality

Analysis of fatalities.—During the ten years 1931–41 seventy-five deaths occurred in the Johns Hopkins Hospital theatres. These cases have been analysed by J. Lyford, Olive L. Berger and H. B. Shumacker, Jun., who conclude that twenty of the deaths were related to the anaesthesia. Of the twenty deaths eleven were thought to have been possibly avoidable; for the remainder an adequate explanation could not be found. In no case was the anaesthetic regarded as being the sole cause of death. Of the eleven possibly avoidable deaths the following were the determining factors: (1) Oedema of the larynx (one case). The patient was a haemophilic with a large haematoma after tooth extraction. The anaesthetic was pentothal sodium. The authors consider that general anaesthesia should have been avoided and that, in any such case, special precautions must be taken to ensure a clear airway. (2) Aspiration of gastric contents (three cases). All were of acute abdominal emergencies and in none of the patients had the stomach been emptied before operation. (3) Spinal anaesthesia (three cases). It is considered possible that the dose was too large or was injected too forcibly or too rapidly. (4) Explosion (one case). An electrocautery was being used on the neck of a patient under open ether. (5) Possible errors of technique in giving an inhalation anaesthetic (three cases). The patients were allowed apparently to become anoxic.

EDITORIAL COMMENTARY—Safety in Anaesthesia

In the administration of anaesthetics an advance would be made if some system of measured dosage could be devised. Many years ago the Special Chloroform Committee of the British Medical Association arrived at certain conclusions regarding the dosage of chloroform. They found that the safety dose for induction was about 2 per cent chloroform vapour, and for maintenance 1 per cent, but that it varied very much and had to be determined in each case. It is well known that the individual variation in reaction to the hypnotic group of drugs is much more common than to any other. Our best guide regarding the dosage for any individual case would be the patient's metabolic rate, but it is doubtful if even such a determination would afford the administrator more than an indication that his patient was to 'take' more or less than the average. We must accept the fact that at present it is impossible to administer a predetermined safe and satisfactory dose, and that our control of the anaesthesia is dependent upon keen observation and correct interpretation of the signs which accompany the various levels of anaesthesia. It is obvious, therefore, that our methods should not impede our ability to recognize at once the important signs as they appear. Particularly is this of importance in controlling the deeper levels of anaesthesia. It has been suggested that recent advances in our methods, although they have greatly facilitated the work of the surgeon and mitigated the discomfort of the patient, have not reduced the frequency of anaesthetic emergencies. It is held by some that ether convulsions is a relatively new condition to be recognized and one that may be related to our newer methods of administration. The fact that cases of ether convulsions occur with a certain frequency in the records of some administrators and not at all in those of others lends support to the view that the mode of administration may be an important factor in their causation.

The administration of a known percentage concentration of anaesthetic gas or vapour cannot be carried out without the employment of a closely fitting face-piece and there may be occasions when the necessary percentage may not be obtainable without curtailment of the oxygen supply. The use of the face-piece makes accurate observation of the patient's condition more difficult and curtailment of the oxygen supply is not without risk of anoxia. We know that complete deprivation of oxygen for a short period produces convulsions. It is not impossible that a partial deprivation for a longer period may have a similar effect. In the large majority of reported cases the anaesthesia is or has been on a deep level when the convulsions occur, and not infrequently it has been reported that gas, oxygen and ether administered by means of a Boyle or similar apparatus was the method employed. It is the opinion of some anaesthetists that when a mixture of gas, oxygen and ether succeeds in inducing a deep anaesthesia with complete abdominal muscular relaxation, the blood contains as high a percentage of ether as if gas had not been used. The gas thus has been a mere vehicle for the ether vapour and has not itself contributed to the anaesthetic properties of the mixture. It would be advisable in such cases to eliminate the gas entirely and not run any risk of curtailing the intake of oxygen. Modern machines are of great value when the lighter levels of anaesthesia are required, but even then they are safe only when in the hands of an administrator who is familiar with the signs of all levels of anaesthesia. This familiarity can best be obtained by means of practice with the mask and drop bottle, and students of anaesthetics are not likely to be safe administrators when they have not received instruction in this method.

It is unlikely that the accumulation and study of statistics would afford a satisfactory answer to the question whether or not modern methods have reduced the frequency of anaesthetic deaths. In the days when chloroform was in routine use it was not difficult to decide that death had been caused by the anaesthetic, for in some 80 per cent of fatal cases death took place before the operation was begun. Today it is not easy to determine to what extent the anaesthetic has contributed to bring about the fatal result. Profound anaesthesia closely resembles surgical shock, if indeed it is not itself a condition of shock. A careful study was made of the reports on 'deaths under anaesthesia' submitted during the last eighteen years by a large general hospital in Scotland in accordance with the instructions of the Crown Authorities. It did not yield any information as regards the value of the different agents and methods used. It served to confirm, however, in no uncertain way, the importance of the skill and experience of the administrator.—ARTHUR MILLS.

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ANEURYSM

See also B I. M P., Vol. I, p. 501; and Cumulative Supplement, Key No. 61.

Dissecting aneurysm

Clinical picture

Post-mortem evidences—Two cases of dissecting aneurysm of the aorta are reported by M. I. Thomas and E. Elizabeth Garber. Both occurred in men aged respectively forty-nine and fifty-four years. The first patient was known to have had a high blood pressure. He was seized at 3 o'clock one morning with severe substernal pain thought to be due to coronary infarction. On admission to hospital he was found to have a moderately enlarged heart with a loud apical systolic murmur and a systolic blood pressure of over 200 millimetres Hg. X-ray examination revealed widening of the aorta. The electrocardiogram showed inversion of the T wave in all leads. During the patient's stay in hospital (twenty-eight days) the pain continued and towards the end became worse. He died suddenly in his sleep. *Post mortem* a dissecting aneurysm was found extending from the distal part of the aortic arch as far as the superior mesenteric artery. Leakage had occurred into the mediastinum where a large clot was present. The second patient was taken ill suddenly with pain between the scapulae and in the abdomen. The systolic blood pressure was over 200. X-ray examination showed widening of the aortic arch and descending aorta. Death occurred suddenly as the result of rupture of the aneurysm, which was found at necropsy to extend to about 2 centimetres above the diaphragm. In both cases the diagnosis was made on the clinical findings of intractable substernal and epigastric pain without fall of blood pressure and on the X-ray evidence of widening of the vessel.

Aneurysm of the pulmonary artery

Clinical picture

Due to syphilis.—S. De Navasquez, who quotes L. J. Boyd and T. H. McGavack's collection of 111 cases of aneurysm of the pulmonary artery, of which thirty-three cases only were due to syphilis, records a case in which a syphilitic male, aged fifty-seven years, showed at necropsy a large saccular oval aneurysm, measuring 6.5 centimetres, which included the left main pulmonary artery. The right pulmonary artery was separate from the aneurysm. The segments of the pulmonary valve were thickened. Both lungs showed coarse fibrous tissue radiating out from the roots, the appearance being that of pulmo lobatum. The liver, weighing 1,690 grammes, showed 'cardiac' cirrhosis with areas of regeneration. The spleen was enlarged and very firm.

Peripheral aneurysm

Surgical treatment of peripheral aneurysms

Clinical types and treatment.—G. H. Pratt considers the treatment, especially surgical, of peripheral aneurysms, and subdivides them as follows. (1) Arterial, which are all acquired: (a) traumatic; (b) degenerative. (2) Arteriovenous. Acquired: (a) traumatic, (b) degenerative; congenital. The symptoms are varied; although all aneurysms form a tumour the contiguous structures, especially when the aneurysm is small, may hide it. Expansile pulsation is present in the early stage but with further elimination of clot the pulsation may be transmitted or even may be obliterated. Pain is a variable symptom, according to the structure compressed by the growing tumour; in the extremities it may be negligible, although in a popliteal

aneurysm pressure on nerves may be responsible for pain and weakness. The pulse distal to the aneurysm may be weak or absent. Congenital aneurysms may be multiple. The ideal treatment in both the acquired and congenital types is excision and end-to-end anastomosis of the vessel; this is more often possible in the traumatic form than is generally supposed. In any treatment of aneurysm in which the main vessel is, or may be, occluded it is most important that stimulation of the collateral circulation should be continued by antispasmodic drugs, external heat and avoidance of trauma; lumbar sympathetic nerve block has its place in the relaxation of spasm.

The commonest cause of acquired arteriovenous aneurysm is a gunshot, stab, airplane or motoring injury. The physiological changes due to arteriovenous fistula are as follows: a fall of blood pressure with recovery, but a greater pulse pressure; an increased pulse rate, greater venous pressure; an increase of cardiac output which depends on size and location of the aneurysm; temporary decrease in size of the heart and artery, then dilatation with hypertrophy of the heart; increased total blood volume; collateral circulation around the fistula. Operation should be postponed for from four to six months from the date of the occurrence of the fistula, in order to permit the above physiological changes to take place. The operative treatment may consist in repair of the arterial wall of the fistula with the wall of a vein. Often the best method is ligation, proximally and distally, of the artery and vein, with excision of the intervening fistula and vessels. It is important to remember, in connexion with the treatment of congenital arteriovenous fistulas, that they are usually multiple and that they may not all be open and functioning at the same time. The treatment of congenital fistulas varies with their size; many small ones, particularly on the face, may be excised surgically, and preferably without the use of a tourniquet. Attention is directed to the tendency of some congenital arteriovenous fistulas to invade and to spread like malignant tumours, necessitating amputation. The author closed eleven such invading lesions, but the patient returned a year later with five new ones.

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ANGINA PECTORIS AND CORONARY THROMBOSIS

See also B F M.P., Vol I, p 547, and Cumulative Supplement, Key No. 62

Angina pectoris

Treatment

Use of testosterone propionate—As a result of previous studies upon a group of twenty-four patients M. A. Lesser reported favourably on the effect of testosterone propionate in angina pectoris. He now reports on a further series of twenty-two patients, twenty-one of them men, treated in this way with equally good results. The drug was given by injection in doses of 25 milligrams at intervals of from two to five days. The number of injections varied from five to twenty-five and averaged eleven. All the first twenty-four patients were benefited by the treatment. The frequency, severity and duration of the attacks were reduced and all the patients were able to increase their physical activity considerably. No ill effects followed the injections and the improvement which resulted was maintained for periods of from two to twelve months after treatment was discontinued. Of the present group of patients, all experienced subjective improvement. In four of them exercise tolerance tests were carried out before and during the treatment. The total number of standard exercises performed by these four patients before an attack occurred was almost doubled, and the subsequent attacks were much shorter. In each case subjective relief was experienced before objective evidence of improvement was obtained.

Coronary thrombosis

Actiology

In industry—H. D. Leinoff records eighteen cases of acute coronary thrombosis due to direct non-penetrating wounds of the chest occurring in the course of industrial employment. The injuries sustained in the eighteen cases were among industrial workers, except in one instance, that of a surgeon, whose chest was jammed against the steering-wheel of his car. These cardiac injuries may be divided into two main groups: (1) direct non-penetrating, and (2) indirect, such as those caused by unusual effort, exposure to gases, increased atmospheric pressure or surgical shock. The second group of cases is to be considered later. In the direct non-penetrating group the most frequent diagnosis has been acute coronary thrombosis with myocardial infarction, but a better diagnostic label would be acute traumatic heart disease with myocardial and pericardial damage. All the patients except one were males and only two were under the age of forty. The chest was injured by heavy objects in 34 per cent of the cases, by striking a hard surface, as in falling, in 40 per cent, and in motoring accidents in 26 per cent. The anterior part of the chest on the left side was the area affected in ten cases, and the back and the left chest was involved in five cases. In a rough estimate the force was moderate in nine cases, rather severe in five cases, and mild in one. External signs of injury were visible in 60 per cent of the cases. The heart may be violently thrown against the bony parts, compressed or torn from its attachments; it may have its cavities burst open or it may

be jarred, as in falling; it may have the blood forced back into the ventricles or prevented from leaving by compression, thus increasing the intracardiac pressure, or it may be bruised by the pressure of fractured bones. The electrocardiographic changes vary and may suggest myocardial or pericardial lesions. The author concludes that the lesion is not rare and may prove non-fatal but disabling; that the clinical picture is that of an acute morbid condition of the heart closely resembling that of coronary occlusion from which it is differentiated by the history; that the history is the most important single factor in determining the causal relation and the subsequent degree of disability; and that this clinical syndrome should be considered in cases of any injury of the chest.

Medico-legal aspects.—F. A. Willius considers that the whole question of the medico-legal aspects of coronary thrombosis requires careful consideration in order to obtain a reliable opinion on which to base decisions in insurance medicine litigation, and in workmen's compensation cases. The matter is rendered urgent by the increasing incidence of coronary thrombosis, and by the establishment of some questionable legal precedents relating to the subject. It should be recognized that coronary thrombosis presupposes coronary arteriosclerosis, which is a universal concomitant factor in the process of ageing. Coronary thrombosis has erroneously been ascribed to strenuous exercise and to heart strain; actually it occurs more often in persons who are engaged in sedentary occupations than among manual labourers, and many cases occur when patients are at rest or are even asleep.

Clinical picture

Atypical cardiac infarction—From 1st January 1941 to 31st March 1942 G. F. Strong observed eleven cases, all confirmed by necropsy, of atypical cardiac infarction. Pain may be absent or merely represented by anginal equivalents such as congestive heart failure, especially of sudden onset, left heart failure, pulmonary oedema or cardiac asthma and sudden changes in cardiac rhythm. On the other hand the symptoms may be cerebral and not cardiac, for example weakness, faintness, collapse, coma, sudden fall in blood pressure, vertigo, nausea, vomiting, psychical disturbance, hypertension, monoplegia or hemiplegia from thrombosis or from cerebral embolism from detachment of a fragment of a cardiac mural thrombus. The cerebral symptoms are more widely recognized as occurring some little time—ten days or so—after the coronary thrombosis, but they may occur at the time of onset of infarction, and may then be due to acute cerebral changes caused by inadequate blood supply. References are made to the records of thirteen cases of atypical cardiac infarction by W. D. Stroud and A. J. Wagner, and to H. M. Pollard and F. H. Harvill's collection of 375 cases of coronary infarction among which 17, or 4.5 per cent, were of atypical cardiac infarction.

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ANOREXIA NERVOSA

See also B.I.M.P., Vol. I, p. 598, and Cumulative Supplement, Key No. 67.

Clinical picture

Report of a case.—Some clinical observations on anorexia nervosa are made by J. M. Berkman. A girl aged sixteen complained of anorexia of eighteen months' duration. There was not any history of psychological disturbance. She stated that she felt distended after small quantities of food. Her weight before the onset of anorexia was 130 pounds. The first menstrual period occurred two months after the onset, since when she had had amenorrhoea. On admission to hospital she weighed 78 pounds. Apart from a low blood sugar (69 milligrams per 100 cubic centimetres) and low basal metabolic rate (−37 and −34 on two occasions), examination was negative. The patient was encouraged to take food and was given desiccated thyroid gland; in three weeks she gained 6 pounds. The initial gain was not maintained; in three months she was readmitted weighing 80 pounds. On this occasion she was not given any thyroid gland preparation, merely a gradually increasing diet and in a month gained 6 pounds. Since then she has been eating normally and her weight when she was last seen was 128 pounds. The basal metabolic rate was −26, −27. The initial gain of weight may be explained by early retention of electrolytes and water. In the succeeding stationary period the excretion of water and storage of flesh probably balance one another. From this time on a constant increase occurs. The fact that the basal metabolic rate rises spontaneously contra-indicates thyroid medication. A similar spontaneous rise in the basal metabolic rate from −16, −17 to −6 was seen in a second patient who did not receive any thyroid gland preparation.

Pathological obesity as a sequel

M. Reiss records the case of a woman aged twenty-two years, who after a disappointment in love, though this did not appear to upset her, lost appetite and her condition was diagnosed as that of anorexia nervosa. Within eighteen months the gross emaciation gave place to pathological obesity. The initial hypofunction of the anterior lobe of the pituitary gland, if this be accepted, was followed by a rapid increase of fat deposition which was not due to

any artificial hormonal treatment by anterior pituitary lobe. The special interest of this case is the demonstration that new hypofunction of the anterior lobe of the pituitary gland can swing to the opposite extreme of hyperfunction in a comparative short time, when once something has occurred to upset its normal balance. Although this is the first time that it has been possible to follow such a development closely, similar behaviour sometimes ensues from infections. Reiss has seen adiposity combined with virilism in girls after an early attack of scarlet fever, a disease which often affects the adrenal cortex. The reverse is sometimes seen as in fat children with raised intracranial pressure whose body shape becomes normal after puberty, or fat girls who become cachectic; but such a rapid swing from emaciation to adiposity has not hitherto been described. The function of the pituitary gland appears to be conditioned by an exact correlation between bodily demands and hormone production, the demands varying according to age and to a variety of constitutional conditions. In the author's case it is suggested that an original hypofunction of the anterior lobe of the pituitary gland became one of pathological hyperactivity. It is also proposed that the designation 'cerebral' pituitary cachexia should be employed in the place of anorexia nervosa.

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ANTENATAL CARE

See also B I. M P., Vol. I, p. 601, and Cumulative Supplement, Key No. 68.

General medical examination

Hypovitaminosis B₁ and E

Incidence in pregnancy.—E. Shute has investigated a series of 580 pregnancies for evidence of deficiency of vitamins B₁ and E. A series of 957 unselected gynaecological cases was used as a control. The requirement of vitamin B₁ is increased about threefold during pregnancy, so that neuritis readily develops, usually in the arm or leg. If recognized and treated early the condition does not progress beyond the stage of numbness and tingling or mild pain, but if the condition is neglected severe polyneuritis or beri-beri may supervene. Vitamin E deficiency is shown by excess of oestrogen in the blood and by threatenings of premature termination of pregnancy which respond quickly to vitamin E administration. Judged by this standard the incidence in the pregnant women of vitamin B₁ deficiency was 17 per cent, of vitamin E deficiency 70 per cent. Of the controls 4 per cent showed hypovitaminosis B₁. Among subjects showing vitamin E deficiency the incidence of vitamin B₁ deficiency was 24 per cent, whereas among the remainder the percentage incidence was only 10. Hypovitaminoses E and B₁ are therefore common in pregnancy and frequently coexist and provide a strong argument for preservation of the germ, the source of both vitamins, in milling cereal grains.

Hygiene of pregnancy

Diet

Analysis of maternal diets.—The dietary habits of 514 pregnant women attending Philadelphia antenatal clinics have been analysed by P. F. Williams and Florence G. Fralin. Compared with the allowances recommended by the National Research Council, the diets of all the women were much below standard. The findings in relation to the more important constituents were as follows. (1) Milk. The percentage of women who consumed the recommended quantity, that is a quart daily, was only 3; the average intake was less than a pint. (2) Potatoes. Two servings daily are recommended but only 3 per cent took this quantity; a further 3 per cent did not eat any potatoes although the majority took under one helping a day. (3) Legumes are recommended for use four times a week in the low-cost diet, three times a week in the moderate-cost diet and once a week in the most costly diet, 48 per cent of the women studied took none at all. (4) Tomatoes, citrus fruits and so on. Two or more daily were taken by 17 per cent, and the majority took some, although in 39 per cent of cases the amount was less than one daily. One portion daily is the minimum recommended. (5) Green and yellow vegetables should be taken at least once a day and twice if possible. Of the women studied 86 per cent took less than two daily servings, and 45 per cent less than one serving a day. (6) Eggs. One a day is recommended; 11 per cent took none, and only 13 per cent reached the standard of one daily. (7) Meat, fish, and similar foods. Most of the women had at least one serving daily. (8) Bread and cereals. The number of women taking these in whole-grain form was determined. Only 17 per cent took as much as half their daily allowance in this form. (9) Fats. 74.5 per cent ate less than an ounce daily of butter or fortified margarine. (10) Sugars. Unrefined sugars such as honey or brown sugar, which are preferable to refined sugar, were taken by only 12 per cent. The results of the inquiries indicate the need for education in the elements of the science of nutrition.

Diet in pregnancy and in the puerperium.—The People's League of Health appointed a committee in 1935 to consider the effect of the nutrition of pregnant and nursing women on maternal and infant mortality and morbidity. In its preliminary report the committee states that the records of 5,022 cases at various London antenatal centres were studied and experiments were made in supplementing the patients' diets. In order to obtain some idea of the type of diet taken by the subjects, nearly 1,000 women were asked to keep a detailed record of their meals during a period of a week. A scoring system was adopted to express the daily consumption of the more important foods, and was found sufficient to reveal any consider-

able deficiencies. None of the diets showed significant insufficiency of first-class protein. A shortage of calcium, due to insufficient consumption of milk and cheese, was noted in about 70 per cent. Iron deficiency was present in 98 per cent. More than half the diets were deficient in vitamin A, nearly half in vitamin B, and half in vitamin C; but the deficiency was considerable only in the case of A. From the data thus obtained the committee decided upon the following daily supplement: saccharated ferrous iron, 18 grains; calcium lactate, 30 grains; traces of iodine, manganese and copper; a preparation of whole vitamin B complex, 15 grains; ascorbic acid, 100 milligrams; halibut-liver oil, 6 minims. The 5,022 women were placed alternately in two groups. One group received the daily supplements, the other acted as a control. Each group was subdivided into primigravidae and multigravidae, and each of these subgroups was again divided into age groups of under twenty-five, twenty-five to thirty and over thirty years. The incidence of pregnancy toxæmia in the various groups was as follows. (1) Primigravidae receiving supplemented diet (1,530 cases), 27.1 per cent; not receiving any supplement (1,512 cases), 31.7 per cent. The difference was most pronounced in the age group twenty-five to thirty years. In the other age groups it was statistically unimportant. (2) Multigravidae. The incidence in both groups was 21.8 per cent. The risk of puerperal sepsis appeared to be unaffected. The incidence of premature delivery was as follows. (1) Primigravidae: treated, 20.1 ± 1.10 per cent; untreated, 23.9 ± 1.10 per cent. (2) Multigravidae: treated, 20.1 ± 1.33 per cent; untreated, 24.2 ± 1.33 per cent. The average birth weight of the babies was not significantly different in the two groups.

Foetal requirements.—At a meeting of the English branch of the Nutrition Society held to discuss nutrition in pregnancy, A. Bourne emphasized the importance of the mother's diet for proper development of the foetus. He attributed to malnutrition much of the blame for the neonatal mortality of 41.7 per thousand in illegitimate infants as compared with 27.7 in normal. Vigour rather than birth weight is influenced by the mother's diet. J. Hammond discussed the competition for food materials between the maternal and foetal tissues, pointing out that if the mother is undernourished her own tissues may be depleted to supply the demands of the foetus. Only severe undernutrition is likely to affect the birth weight. J. Barcroft brought forward evidence of a selective action in the transference of food materials and suggested that the size of the foetus may be related to that of the placenta. T. Moore described experimental work showing that transfer of vitamin A to the foetus is very limited, but H. Hoch stated that the amount of the vitamin in foetal blood is the same as that in the maternal blood; on the other hand, carotene is found in much larger amount in the maternal than in the foetal blood. M. Balfour stated that supplementing the diet of pregnant women in depressed areas had produced improvement, as compared with controls, in both mothers and infants. H. M. Sinclair thought that the importance of anaemia in pregnancy had been exaggerated because of failure to allow for pregnancy hydraemia; but Lucy Wills pointed out that decrease in haemoglobin is often unaccompanied by decrease in the erythrocyte count. G. Bourne said that infantile mortality and still-birth rates are lowest in the best fed countries. E. J. Bigwood cited evidence from Belgium that the poor diet now available has not affected the birth weight of infants.

Nutritional deficiencies during pregnancy.—An Annotation in the *Lancet* reports a meeting of the Scottish Group of the Nutrition Society in December, 1942, at which H. M. Sinclair reviewed the evidence relating to nutritional deficiencies during pregnancy. Supplementary feeding with vitamins A and D has been thought to lower the incidence of puerperal sepsis but it is doubtful whether the action of the vitamins is specific. Conflicting reports have been made on the effect of the vitamin B complex in preventing the toxæmias of pregnancy, gestational polyneuritis and Wernicke's encephalopathy. The claim that vitamin E prevents abortion is not yet confirmed, nor is it established that vitamin C or vitamin K, or both, may play a part in preventing accidental haemorrhage during pregnancy and excessive bleeding during parturition. Hyperplasia of the gums is not uncommon during pregnancy but does not yield to treatment by vitamin C; it may be due to excessive quantities of oestrogen in the tissues. Anaemia due to iron deficiency is often seen in pregnant women, but the physiological hydraemia of pregnancy must be taken into account when assessing the severity of the anaemia. The maternal calcium reserves are encroached upon during the second half of pregnancy to satisfy the demands of the foetus, but the addition of calcium to the diet may have the disadvantageous effects of prolonging pregnancy and of hardening the infant's skull. D. Baird thought that differences of diet are probably responsible for the higher rates of still-births and of premature labours in hospitals as compared with those in private specialist practice. The diets of pregnant women often fall below the standard set up by the League of Nations commission, and evidence is accumulating that prematurity and still-birth rates can be lowered by raising diets to the above standard. I. Leitch thought that dietetic deficiencies were probably to blame for the fact that the still-birth and neonatal death rate in Scotland (80 per 1,000) so much exceeds that for England and Wales (66 per 1,000) and for New Zealand (51 per 1,000).

Protein, mineral and vitamin requirements.—Muriel E. Bell emphasizes the special nutritional requirements of the pregnant woman. The saying that she must 'eat for two' is to be interpreted qualitatively rather than quantitatively. (1) Total caloric intake: the increase in the later months should not exceed 25 per cent. (2) Protein is required to build up the foetus, the uterus and the placenta. The mother also stores protein in considerable quantity and a good

supply of stored protein probably favours lactation. Evidence has been adduced against, and none for, the theory that a high protein intake may cause pregnancy toxæmia. (3) Mineral salts. Iron must be provided to satisfy the demands of the foetus in utero and up to the time of weaning, and to compensate for impaired absorption resulting from the hypo-acidity normally associated with pregnancy. Calcium must be kept up to an optimal level, preferably by giving milk; skimmed milk may be used if the mother tends to get too fat. In some countries iodine is necessary and may be given in iodized salt. (4) Vitamins. Milk, eggs or butter in sufficient quantity will provide vitamin A. Vitamin B₁ is particularly necessary; deficiency may result in polyneuritis, prematurity and, in cases of heart disease, in acute heart failure. B₂ must also be supplied. Adequate vitamin C intake is thought to guard against post-partum hæmorrhage. Vitamin D is required for the formation of the foetal bones and teeth, and should be supplied in the form of fish-liver oil.

Relation of maternal diet and health of foetus.—Attention is drawn in a Leading Article in the *British Medical Journal* to the recent awakening of interest in the problem of saving infants' lives. The demand is now almost universally supported that the foetus in utero should, during the last three months, count for rationing purposes as an independent organism. In Toronto a study has been made of three groups of pregnant women; (1) a 'poor diet' group, (2) a group on a similar diet supplemented during the second half of pregnancy, and (3) a group consisting of women who were taking a 'moderately good' diet and were able to pay for a recommended 'good' diet. The standard daily diet prescribed by the Toronto workers contained the following quantities of essential foods: milk two pints, cheese one ounce, butter and meat 'an average portion', vegetables in addition to potatoes two servings, one egg, one orange or equivalent, two teaspoonfuls of cod-liver oil or equivalent, two tablespoonfuls of wheat germ. Half the cereals and bread had to be taken in whole-grain form, liver to be eaten once a week; salt to be iodized; iron to be taken if indicated. The percentages of pregnancies ending in miscarriage were as follows: poor diet group 6, supplemented group 0, good diet group 1.2. Of threatened miscarriage the respective percentages were 8.4, 1.1 and 2.4. Premature delivery occurred respectively in 8, 2.2 and 3 per cent, still-births in 3.4, 0 and 0.6 per cent, and toxæmia in 7.6, 3.4 and 3 per cent. The average birth weight of the babies for the poor diet group was 7 pounds 10 ounces, for the supplemented group 7 pounds 7 ounces and for the good diet group 7 pounds 6½ ounces. Of the first 250 babies frequent colds occurred in 21 per cent of the poor diet babies; in each of the other two groups the percentage was 4.7. The corresponding figures for pneumonia were 5.5, 0.5 and 0.9; for rickets 5.5, 0 and 0.9; and for anaemia 25, 9.4 and 17.1 per cent. The authors conclude that mothers on better diets have better health and fewer complications, and are better obstetrical risks, and that their babies are healthier. More of them are able to breast-feed their babies; the respective percentages of breast feeding for the three groups were 81, 95 and 88 while the patients were in hospital, and 59, 86 and 71 at six weeks after delivery.

EDITORIAL COMMENTARY—Diet in Pregnancy

Recent years have witnessed a great intensification of interest in the subject of diet in pregnancy. The experimental studies by the Mellanbys and other workers in the two decades before the present war have been supplemented by several clinical studies during the last five years.

Certain conclusions can be accepted already. There can be no doubt, for example, that the diet of pregnant women even of the better class leaves much to be desired. R. A. McCance, E. M. Widdowson and C. M. Verdon-Roe (1938) studied the diets of 120 pregnant women in Great Britain at different economic levels varying from wives of unemployed miners to women of the professional classes. It was found that whereas the intake of calories was little affected by income, the consumption of milk, fruit, vegetables, meat and fish rose with income. Intake of calcium, phosphorus and iron also rose with income but the average intake even of the well to do was much below probable requirements and only one of the 120 women was taking enough calcium and phosphorus. Among the three lowest income groups, including all who had less than 25s. per head weekly left after deducting rent, the calcium intake was less than one-third of the required amount. That of iron was suboptimal in all, that is it was below 20 milligrams daily. From the above study it is clear (1) that the poorer women cannot afford a diet which is sufficient for the needs of pregnancy, and that their income needs to be supplemented either in the form of food or money; (2) that it is not enough to tell pregnant women in the better-off classes to 'eat a good mixed diet' or to 'continue to eat what they have been accustomed to'. Even in the latter classes it is necessary to ensure that the women get sufficient calcium, phosphorus, iron and vitamins.

Reliable experimental and clinical evidence has demonstrated the great importance of calcium and vitamin D to both mother and child. If the substances are present in insufficient amounts in the mother's diet the young may be born with a tendency to rickets and to defective teeth—a tendency which it may be impossible to overcome by adequate feeding after birth. Calcium is best supplied in milk, and although vitamin D is present in milk, butter and green vegetables, the amount thus furnished may be considerably less than is required, especially in winter. To ensure that the intake is sufficient it is advisable to give fish-liver oil. The provision of free milk and fish-liver oil for expectant mothers by the public health authorities is a wise measure, the cost of which is certain to be repaid over and over again in the better health of the coming generation.

Sweeping claims have been made, too, regarding the effect of diet in preventing various ills of pregnancy such as miscarriage and premature birth, toxæmia, uterine inertia and puerperal sepsis. Such claims, made somewhat vaguely for some years, have received support from two recent reports—that of J. H. Ebbs, F. F. Tisdall and W. A. Scott (1941) in Toronto and that of the People's League of Health in Britain. The Toronto results are startling and certainly call for serious consideration. The numbers involved in the experiment are, however, small and for that reason it should be repeated on a much larger scale. The People's League of Health experiment is not open to this objection for comparatively large numbers of women were used. Although the incidence of toxæmia in primigravidae who received the dietary supplement was significantly less than in the controls, the degree of significance was not great, and there was a $2\frac{1}{2}$ per cent possibility that the result might be due to chance. In multi-gravidae, although the incidence of toxæmia was also less in the treated women than in the controls, the difference was not large enough to be of statistical significance. This is strange and must be disconcerting to those who claim from either or both experiments that a dietary deficiency is the cause of pregnancy toxæmia since there is not any reason to assume that toxæmia has a different aetiology in primigravidae and multi-gravidae. In this connexion it should be noted that R. A. Ross, W. A. Perlzweig, H. M. Taylor, A. McBryde, A. Yates and A. A. Kondritzer (1938) did not find much difference in the incidence of toxæmia by supplementing a diet that was regarded as marginal by the addition of dried milk, vitamins A, B, D and E, calcium and iron. Since the women were resident in a charitable institution it was certain that the supplements were actually consumed.

In Hong Kong the incidence of eclampsia in patients suffering from avitaminosis B₁ (beriberi) is about fifty times the normal and consequently a considerable amount of work has been done on the possible part played by vitamin B₁ in the causation of toxæmia. Space does not permit discussion of the matter but the results of investigations are contradictory and an adequate explanation of the Hong Kong experience has not yet been given.

While awaiting the results of further investigation the practitioner cannot do better than advise the Mellanby diet in so far as war-time restrictions permit: two pints of milk daily; one or two substantial servings of green vegetables, cabbages, spinach or lettuce daily, one or two eggs or egg yolks daily; an apple or orange, or some fresh fruit daily; sea fish twice or more a week; calf's liver once a week; cod-liver oil, two teaspoonfuls daily or, if this is objected to, an equivalent amount of halibut-liver oil. If there is any suspicion of anaemia iron in medicinal form should be administered.—F. J. BROWNE.

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APPENDICITIS

See also B.E.M.P., Vol. I, p. 729; and Cumulative Supplement, Key No. 75.

Acute appendicitis

Aetiology

Acute appendicitis in persons over fifty.—J. H. Powers analyses a series of forty cases of acute appendicitis in patients of fifty years of age and upwards and compares it with a group of 228 patients under fifty. The proportion of older patients to the total number was as follows: simple acute appendicitis 5.4 per cent; gangrenous appendicitis 11.3; with local peritonitis 9.1; with perforation and local peritonitis 25.7; with perforation and general peritonitis 32.0; with abscess 30.3. Thus the serious complications, peritonitis and abscess, are considerably commoner in older patients. The symptoms and signs may be atypical, but in the series under consideration they were similar to those occurring early in life. The mortality was much higher in the older group—17.5 per cent compared with 2.1 per cent. Often death was due to the risks which occur in any operation on elderly patients, namely pulmonary complications and cardiovascular accidents, rather than to the disease itself. The fact that acute appendicitis in elderly people is apt to be fulminating in character, progressing rapidly to gangrene and perforation, increases the importance of early operation. The cause in many cases is appendicular obstruction. Little evidence has been obtained in support of the theory that vascular disease is an aetiological factor.

Pathology

Enterobius (oxyuris) vermicularis.—J. R. Schenken and Emma S. Moss report their observations on 1,000 surgically removed appendices at New Orleans, by the adoption of a stand-

ardized procedure of examination used by parasitologists, as regards the appendicular presence of *Enterobius (oxyuris) vermicularis*. The total incidence in the 1,000 appendices was 23·3 per cent; but the authors believe that the percentage of 31·2 found in the last 400 appendices examined was a more accurate figure. The contents of the 400 appendices (group 2) were centrifuged until the resultant emulsion gave a clear residue more suitable for microscopical examination than the emulsion from the first six hundred appendices (group 1) in which the centrifugalization occupied one minute only. In group 2, white females contained parasites in 42 per cent of cases, negro females in 10 per cent; in white males parasites were present in 38 per cent of cases, and in negro males in 13 per cent. An appendix from a white patient is about three to four times more likely to be infected than one from a negro, but the reason for this is not known. In the same series a search was made for all other forms of intestinal infestation; *Trichocephalus trichiurus* ova, *Strongyloides stercoralis* larvae, *Necator americanus* ova, *Hymenolepis nana* ova and *Taenia* ova were more common in whites; but *Ascaris lumbricoides* were almost as numerous in whites as in negroes.

Clinical picture

Analytical observations.—W. Duley presents an analysis of 417 cases of acute appendicitis. The youngest patient was only a year old; the oldest was aged eighty-one. The largest number of cases (141) occurred in the second decade of life and 87 per cent occurred within the first four decades. Pain in the epigastrium, in the umbilical region or in the whole abdomen, which later became localized in the right lower quadrant, was present in 72 per cent. In practically all the patients pain in the lower quadrant was a characteristic feature; vomiting occurred in 69 per cent. Tenderness in the right lower quadrant was observed in all but three cases, and rigidity was present in 75 per cent. A history of previous attacks was given in 26 per cent. The cases were grouped as follows. (1) Unruptured appendix (300 patients), treated by immediate operation; (2) ruptured appendix with spreading peritonitis (seventy cases), treated by operation after a delay to allow of restoration of the fluid and electrolyte balance; (3) ruptured appendix with abscess (forty-seven cases), treated by delayed operation. The average temperature was 99·7° F. in the first group, and 101·2° F. in the second and third groups; the average pulse rates were 77, 107·9 and 100·1 respectively; the average leucocyte count was 15,400 with 83·7 per cent polymorphonuclear leucocytes in the first group, 18,000 with 86·7 per cent polymorphonuclear leucocytes in the second group and 17,100 with 84·3 per cent polymorphonuclear leucocytes in the third group. Drainage down to the peritoneum was employed in many of the cases of unruptured appendix, and intraperitoneal drainage was employed in all but two cases when the appendix had ruptured. When intraperitoneal drainage was employed the wound was usually left unsutured except for suture of the peritoneum. In the cases of ruptured appendix gastric suction was begun immediately after operation, poultices were applied to the abdomen and infusions and transfusions were given; sulphonamide compounds were given to some of the patients. In three cases of appendix abscess the organ was not removed. The mortality rate for the entire series was 3·3 per cent. For the first group it was nil, for the second group it was 14·2 per cent, and for the third group 8·5 per cent. In all the fatal cases the average interval between the onset and admission to hospital considerably exceeded the general average for the group concerned. Apart from one case of pulmonary embolism local complications were the cause of death in all cases. Non-fatal complications occurred in 9·6 per cent of the cases in group 1, in 44·3 per cent of cases in group 2 and in 40·4 per cent of cases in group 3.

Anomalies in the clinical picture.—C. E. Gardner, Jun. and C. J. Sapp point out that in the text-book picture of the acutely inflamed unruptured appendix the symptoms develop suddenly in an apparently healthy young adult, beginning with pain, usually in the epigastrium, which later becomes localized to the right lower quadrant. Pain is followed by nausea and perhaps vomiting, by constipation, moderate fever and leucocytosis, with tenderness and muscular spasm in the right lower quadrant. In a group of 500 cases, nevertheless, they found that one in every fifteen patients was over fifty or under ten years of age. A considerable proportion were suffering from some other disease when the attack occurred. Pain was not the first symptom in one in every twelve cases. The character and site of the pain varied. In 125 of the cases the initial pain was not located in the centre of the abdomen; in a few it was felt in the back or chest. In 10 per cent it never became localized. One in every six patients had neither nausea nor vomiting. Constipation was present in only thirty-four of the patients; many were operated upon before there was time to discover whether they were constipated or not. Thirty complained of diarrhoea; in some this occurred after the taking of a purgative. The rectal temperature was normal in 22 per cent. Twenty-four patients had temperatures of over 102° F. Two in every fifteen patients had a leucocyte count of under 10,000. Tenderness was present in all cases; muscular rigidity in only 7 per cent.

Closed loop intestinal obstruction.—As pointed out in an Annotation in the *Lancet*, the conception of acute appendicitis as an example of closed loop intestinal obstruction increases the responsibility of the doctor for early diagnosis, but it also makes it easier for him to follow the course of events. In the classical case the initial symptom is pain of a colicky character which is generalized or situated in the epigastrium or umbilical region. With the shift of the pain to the right iliac fossa its character alters, and it becomes continuous. In the early stages the patient wants to move about, but the continuous pain soon makes him want to lie still. Tenderness is at first over the appendix, so that the site varies with the

position of the latter. It may be elicited only on rectal or on vaginal examination, or, in the case of a high retrocaecal appendix, in the hypochondrium or loin. In the next stage the appendix becomes inflamed and, if the tip is not wrapped in omentum and happens to touch the abdominal wall, an area of hyperaesthesia to pinprick appears. With a high retrocaecal appendix this area may be in or near the renal angle; with a pelvic appendix it is absent. Guarding of the muscles is a reflex produced when the parietal peritoneum is pressed down upon the inflamed appendix. It is commonly absent when there is a pelvic appendix. Rigidity is present before the hand is laid on the abdomen and this sign signifies peritonitis. Leucocytosis is a late sign, indicating that rupture and peritonitis have occurred.

Treatment

Importance of prompt surgical intervention in children.—A Leading Article in the *Lancet* draws attention to the fact that there is greater urgency in appendicitis in children than there is in adults. Intraperitoneal infection is less likely to remain circumscribed in the child; discrete abscess formation should never be expected and if an abscess does form it may leak or burst. The reasons are that the omentum is relatively short and the leucocyte reaction relatively slight. The child with abdominal pain is usually reliable evidence and in general the course of the case can be traced with ease. The two conditions to be wary of are (1) the pelvic appendix with tenderness only on rectal examination, without any signs on abdominal palpation and often with a history of diarrhoea, and (2) the high retrocaecal appendix which may mimic renal disease. It must be remembered that appendicitis is the only important cause of persistent abdominal colic in a child, and when this colic is followed by pain on the right side of the abdomen the case must be regarded as one of appendicitis and the patient treated by prompt surgical intervention. Operation should never be delayed unless the attack is obviously subsiding, in which event delay may be considered. The administration of sulphanilamide intraperitoneally at the time of operation, and afterwards by mouth or parenterally, appears to improve the prognosis.

Value of health education.—Some observations by D. B. Armstrong of the Metropolitan Life Insurance Company of New York witness to the value of health education in reducing the mortality rate of acute appendicitis. His experience covers some 17,000,000 policy holders in the United States of America and in Canada, a group sufficiently representative of the populations of the two countries. In the period 1912–1942 the mortality from acute appendicitis showed a steady rise up to about 1932 and since then a decline which has recently become accelerated. This decline occurred in spite of the fact that the incidence has apparently increased. The factors believed to be chiefly responsible for this improvement are education and chemotherapy. During the seven years prior to 1940, when the former factor was operating alone, the mortality rate among policy holders fell from 13.2 per 100,000 in 1933 to 10.3 in 1939, a reduction of about 22 per cent. The Metropolitan Life Insurance Company led the way in an educational approach to the public. Numerous methods were used to arrest the policy holder's attention and to teach him simply and dogmatically that for persistent abdominal pain the doctor should be called and laxatives eschewed. The message was spread by the Company's agents, by use of commercial advertising space and in other ways. The Company believes that the financial saving in death claims has covered many times over the outlay incurred. Since 1940 chemotherapy has reinforced propaganda and the mortality rate has fallen to 5.5 per 100,000, a decline since 1933 of 58 per cent.

Chronic appendicitis

Diagnosis

The ileo-gastric syndrome—The ileo-gastric syndrome, which was chosen by L. R. Braithwaite as the subject of the 1941 Moynihan lecture, results from chronic lesions in the ileo-caecal angle, including chronic appendicitis, chronic simple ileo-caecal adenitis and chronic tuberculous adenitis. (1) In appendicitic dyspepsia the patient, who is usually young, complains of epigastric discomfort or of pain which may precede or follow meals and is variable in frequency and in severity; gastric flatulence is also present and tenderness over the ileo-caecal region is common. Haematemesis occurs rarely. Gaseous distension of the caecum and referred epigastric or umbilical pain on pressure over the appendix are observed in about 30 per cent of cases. The test meal reveals moderate hyperacidity and absence of bile three hours after meals, indicative of pyloric spasm. X-ray examination reveals pylorospasm (delayed gastric evacuation with increased peristalsis) in 40 per cent of cases; delay in filling of the caecum and appendix due to spasm of the ileo-caecal valve; delayed emptying, abnormal filling or fixation of the appendix associated with local tenderness on pressure; and ileal stasis. (2) Simple chronic adenitis, with a mass of glands in the ileo-caecal angle, is seen in young adults. The condition is characterized by exacerbations, with fever, and by local tenderness, with 'indigestion' resembling appendicitic dyspepsia but less severe. X-ray examination shows spasm of the lower ileum and ileo-caecal valve. Operation is inadvisable if it can be avoided, but the differential diagnosis from appendicitis may be impossible, especially in the more acute exacerbations which are seen most often in children. It is not certain that the appendix is the primary cause of the adenitis; the lower ileum and caecum may be involved. (3) In chronic tuberculous adenitis symptoms probably arise from local peritonitis set up by the irritation of a calcified gland. Massage or violent exercise may cause an exacerbation. In the quiet intervals spasm of the ileo-caecal valve and pylorospasm are revealed by X-ray examination and by a test meal in about 30 per cent of cases, and localized spasm of the ileum may

also be observed. Calcified glands are visible in the radiograph. The three conditions can be distinguished from one another by X-ray examination. Gastric signs observed at operation are pyloric spasm, pyloric congestion and enlargement of a gland on the greater curvature near the pylorus. The cause of the syndrome is undetermined. The lymphatic theory postulates a flow of infected lymph from the ileo-caecal to the gastric region, the nervous theory suggests a sympathetic reflex of a protective character.

Tumours of the appendix

Carcinoid tumour

Adenocarcinoma with metastases. --R. A. Hopping, M. B. Dockerty and J. C. Masson record the case of a woman, aged forty-seven years, with a primary carcinoid tumour of the vermiform appendix with extensive metastases in the abdomen, especially in the right ovary. The name, carcinoid tumour, was first used in 1907 by S. Oberndorfer. These tumours have been widely regarded as being benign or as grade I adenocarcinomas (Broders). In addition to their case of carcinoid tumour of the appendix with metastases, Hopping, Dockerty and Masson collected sixteen similar tumours with metastases, which therefore might deserve the name adenocarcinoma rather than carcinoid tumour.

EDITORIAL COMMENTARY—Diagnosis and Treatment of Appendicitis

The sequence of events in the typical case has been rightly stressed since Murphy first gave his classical description. para-umbilical colicky pain accompanied by nausea or vomiting and followed by a gnawing aching pain and tenderness in the right iliac fossa. Variations in the sequence necessarily throw doubts on the diagnosis and suggest other conditions, but it should ever be borne in mind that appendicitis is the commonest acute abdominal disease and it must be absolutely excluded, especially in children, before a complacent attitude is adopted. In the examination of patients suspected to be suffering from acute appendicitis it appears to be very commonly forgotten that the acutely inflamed appendix is an extremely tender organ. If therefore a point of extreme tenderness can be found in any of the situations occupied by the appendix it is strong presumptive evidence, in conjunction with other signs and symptoms, of the disease. It only remains for the doctor to remind himself that if such tenderness is missing from the right iliac fossa it may be either deep in the pelvis and obvious on rectal examination, or high up in the loin in the neighbourhood of the right kidney. Attempts have been made to aid diagnosis by a leucocyte count, although the delay which may be necessary for a comparison in some cases, and the variability in response in different types of case, render it of doubtful value. A more interesting type of investigation is the cytological reaction in peritonitis. This and the bacteriology of the infection may have great significance in the use of the sulphonamides in the future.

During the past four or five years, and particularly during the present war, the tendency has been for most writers to emphasize operative treatment no matter at what stage the disease may be. In cases in which the appendix is unperforated there is no disagreement at all, but when the patient is rendered gravely ill by delay, from one cause or another, modern methods of pre-operative treatment have greatly discounted the dangers of operation. Patients with localized or diffuse peritonitis will nearly always show a great improvement after a few hours of preparatory resuscitation treatment. Distension and its accompanying nausea or vomiting are rapidly relieved by a duodenal suction tube or a Miller-Abbott tube; inhalation of oxygen by a B.L.B. mask helps by replacing non-absorbable nitrogen and inhibiting growth of anaerobes; intravenous drip saline and glucose restores the fluid balance and loss of chlorides; pain and shock are counteracted by warmth applied through hot water bottles and blankets or by radiant heat from electric lamps in cages; enemas and peristaltic stimulants are contra-indicated. As soon as the patient's condition permits, and generally within a few hours, the necessary operative measures can be taken. The actual scope of the operation will depend upon many factors, local and general, the essential point being to avoid doing anything more than is justified by the patient's general condition. Incising an abscess or draining the peritoneal cavity may be all that should be attempted, but in other cases an appendicectomy can be carried out without any undue risk.

The post-operative treatment in these difficult cases is on the same lines, aided by the judicious and sparing use of small doses of morphine. Recently it has become clear that sulphonamides are being increasingly used in the post-operative treatment of suppurative cases and although it is impossible to give any comparable statistical evidence, many surgeons claim that there is a reduction in the mortality rate. A limited personal experience suggests that there is lessening of the incidence of suppuration in the wound in cases in which drainage is required. Oral, parenteral and local administration have all been advocated.

In spite of doubts expressed by some writers, the general view still holds that the treatment of appendicitis in children is that of operation as soon as the diagnosis has been made. The failure of localization of the inflammatory process, and the lack of resistance in children to dehydration and prolonged toxæmia, remain potent arguments against delay at any stage. For the same reasons, in toxic cases, the necessity for measures of resuscitation is even greater than in adults.

The McBurney incision still appears to be considered the most generally useful although the Rutherford Morison muscle-cutting incision is increasingly popular, especially in cases of abscess. Many ingenious methods of dealing with the stump of the appendix have been

suggested, based on theoretical objections to the common method of ligaturing the stump and burying it by a purse-string suture. In an experience of well over a thousand cases, I have never seen any trouble resulting from this method, which is simple and safe.

From time to time, closure of all incisions without drainage is advised, except in cases of localized abscesses. The question of drainage, however, requires considerable judgment, and it is an extremely sound rule to drain when in doubt. The tube can always be removed after twenty-four hours if all goes well, but it takes a great deal of moral courage to insert a tube twenty-four hours after the original operation if things are going wrong—and it may be too late. If there has been any difficulty in removing the appendix, and especially if there has been any venous oozing afterwards, this should be regarded as an indication for drainage —

H. C. WARDLEWORTH NUTTALL.

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APRAXIA

See also B.E.M.P., Vol. II, p. 1.

Clinical picture of all types

Clinical examination

Limb-kinetic, ideokinetic and ideational apraxia—A case of bilateral apraxia is described by H. A. Teitelbaum, O. R. Langworthy and A. B. King. The patient showed all three of Liepmann's types of apraxia, limb-kinetic, ideokinetic and ideational, he was a negro, aged sixty-seven, who was admitted to hospital complaining of weakness of the right arm. He could answer only a few simple questions and had difficulty in finding words and often used them incorrectly. Examination revealed slight weakness of the right lower part of the face, restricted mobility of the right shoulder, slight weakness of the right arm and severe weakness with slight spasticity of the right leg. Fine movements could not be performed with the right arm; voluntary movements were athetoid in character. The abdominal reflexes and ankle-jerks were absent; other reflexes were present although the arm reflexes—except the right biceps reflex—were weak. Babinski's sign was elicited on both sides. Vibratory sense was lost below the pelvis on the right side and below the knee on the left, with slight loss of pain sense in the right leg. Two-point discrimination and stereognosis were lost in the right hand. Sensation was otherwise normal. Apraxia of both arms was present; the man carried out some acts correctly on request, but made many mistakes such as attempting to 'strike' his thumb instead of the match on a matchbox. Tests for syphilis were positive in the blood and cerebrospinal fluid. Three months later the patient suddenly lost consciousness, clonic spasms occurred in the left arm and he died the next day. Necropsy showed bilateral pneumonia and syphilitic aortitis. The left middle cerebral artery and both anterior cerebral arteries were thrombosed. Extensive atrophy due to softening was found in the left supramarginal and post-central gyri and smaller areas of recent softening were present in the centrum ovale of the left frontal lobe, involving the corpus callosum. The fact that apraxia is associated (as in this case) with focal lesions does not prove the existence of a centre for eupraxia. The associated action of various parts of the cortex is the basis of complex purposeful movements and any lesion that disorganizes the association may result in apraxia.

Teitelbaum, H. A., Langworthy, O. R., and King, A. B. (1942) *Arch. Neurol. Psychiat., Chicago*, 48, 469.

ARGYLL ROBERTSON PUPIL

See also B.E.M.P., Vol. II, p. 6.

Pseudo Argyll Robertson pupil

Aetiology

Adie's syndrome—J. B. Dykes draws attention to the frequency with which Adie's syndrome is mistaken for syphilis of the central nervous system, even in the absence of serological confirmation. The characteristics of the above symptom-complex are absence of tendon reflexes and anomalous pupil reactions, consisting in delayed or slow but exaggerated response to accommodation and sometimes to light, with equally slow dilatation after the stimulation has ceased. This so-called tonic pupil is usually present on one side only, but may be bilateral, and is usually larger than the normal pupil. It reacts in the usual way to atropine and physostigmine but it is constricted by acetyl- β -methylcholine chloride which has not any effect on the normal pupil. The reflex responses which are most often unobtainable are the Achilles and patellar jerks, but all tendon reflexes may be absent. Sensory disturbances do not occur.

Variations of the fully developed syndrome are seen. The aetiology is unknown; instability of the autonomic system associated with emotional disturbances has been suggested as being the immediate cause, and eight cases reported by the author support this conception. The condition is usually discovered by chance, but visual symptoms are occasionally complained of. No treatment is known or required, but many of the patients are depressed and anxious, having been told that they have a serious disease; they may need psychotherapy.

Dynes, J. B. (1942) *J. Amer. med. Ass.*, **119**, 1495.

ARRHYTHMIA

See also B.E.M.P., Vol. II, p. 10; and Cumulative Supplement, Key Nos. 78-85.

Tachycardia

Paroxysmal tachycardia

Electrocardiographic observations.—That caution should be observed in making a diagnosis of serious heart disease when inversion of the T waves is the only abnormal finding is shown by the following case, reported by G. M. Currie. The patient, a girl aged thirteen, was admitted to hospital in an attack of paroxysmal tachycardia which lasted thirty-six hours and then, having defied all treatment, stopped spontaneously. The first attack had occurred three years previously and since then the patient had had six attacks, lasting from two to twenty-four hours and leaving her well but feeling weak for some days. Examination on admission showed that the heart was not enlarged either clinically or radiologically; a systolic murmur was audible to the left of the sternum. At the end of the attack the electrocardiogram showed a lowering of the S-T interval and inverted T₂ and T₃ waves. Four days later slight inversion of T₁ was also present. The child was kept at rest in bed for eight days. One month after the attack the electrocardiogram was normal. Some months later electrocardiograms were obtained during and after an attack which lasted three hours; the findings were similar but less pronounced, with a return to normal a month after the attack. Treatment was directed to improving the child's psychological condition. No further attacks have occurred during a period of twenty months during which she has remained under observation. The transient alterations in the T waves in such a case as this appear to indicate merely temporary exhaustion or overstrain of the heart muscle.

Currie, G. M. (1942) *Brit. Heart J.*, **4**, 149.

ARTERIAL DISEASE AND DEGENERATION

See also B.E.M.P., Vol. II, p. 39, and Cumulative Supplement, Key Nos. 86-93

The mechanism of the arterial circulation

Collateral circulation

Experimental devascularization of the stomach.—In the Louis Gross Memorial Lecture on 21st October, 1942, before the Montreal Clinical Society, B. P. Babkin, J. C. Armour and D. R. Webster described their experimental results obtained in dogs, bearing on the restoration of the functional capacity of the stomach when deprived of its main arterial blood supply. This appropriately chosen subject carries on the work done by Louis Gross on the improvement in the cardiac circulation brought about by ligation of the coronary sinus, which minimizes the tendency to the formation of a cardiac infarct after a sudden and complete occlusion of the anterior descending branch of the left coronary artery. M. Fauteux, a follower of Gross and one of the author's co-workers in the physiological department, found a simpler method of improvement of the coronary circulation, namely by ligation of the vena magna cordis; this procedure was based on experiments on dogs and was later applied to human beings suffering from coronary artery disease. The main conception of Fauteux was the close resemblance between arteriosclerotic disease of the coronary vessels and that of the blood vessels of the extremities. W. A. Oppel of Leningrad seems to have been the first surgeon to ligature the popliteal vein in the treatment of senile gangrene of the feet. The benefit from venous ligation was presumably due to the rise of the arterial and venous blood pressure in the vascular bed below the arterial and venous obstruction and to the development of a collateral circulation. The main theme of the lecture—the effects of partial devascularization of the stomach—is then described. Whereas ligation of all the arteries and veins of the stomach in the dog causes gangrene of the stomach and death of the animal, partial devascularization affects the secretory function very little. After ligation of the main gastric arteries the arteries become greatly enlarged, with new anastomoses and adhesions to spleen, kidneys, pancreas and intestines. The stomach resists the reduction of the arterial blood supply better than does the heart and much better than does the brain. Permanent damage of the gastric secretion or motor function does not occur after almost complete de-arterialization. Ligation of most of the arteries supplying the stomach never leads to the formation of a peptic ulcer. In cases of profuse gastric haemorrhage one or two arteries nearest to the bleeding-point may be ligatured without risk of gangrene of the gastric wall or of peptic ulcer.

Periarteritis nodosa

Aetiology

Effect of renal insufficiency.—R. L. Holman in a series of papers on experimental necrotizing arteritis in dogs draws attention to the resemblance of the lesions produced experimentally

by injections of uranium nitrate and of mercuric chloride, and as the result of bilateral nephrectomy. In this connexion it is interesting to note that many human cases of periarteritis nodosa are preceded by diffuse glomerulo-nephritis. A survey of the twenty cases of periarteritis nodosa in the files of the Department of Pathology of Columbia University substantiated this view by showing that in twelve of these twenty cases there was definite evidence of nitrogen retention, and that in the majority the renal insufficiency antedated the arterial changes.

Is anaphylaxis a cause?—A. R. Rich and J. E. Gregory describe experiments designed to elucidate the aetiology of periarteritis nodosa. Having observed at necropsy typical lesions of this condition in a series of cases of serum sickness or sulphonamide reaction, they determined to investigate the results of similar sensitivity reactions in rabbits. One group of nine animals received a single intravenous injection of 10 cubic centimetres per kilogram of horse serum; another group of five animals received the same dose of serum plus seven to ten daily doses of sulphadiazine 0.5 gramme per kilogram orally. All the rabbits became hypersensitive to serum as shown by skin tests and subsequently received further doses of serum or sulphadiazine or of a combination of the two. As the animals died or were killed in the course of the experiment necropsies were performed. All showed the lesions of periarteritis nodosa in various stages of evolution. The authors suggest therefore that periarteritis nodosa is an anaphylactic phenomenon.

Chronic arteritis

Arteriosclerotic endarteritis

Sympathectomy.—H. R. Ives reports under the heading of 'lumbar procaine block and sympathectomy in arteriosclerotic endarteritis', seven cases in which, contrary to previous opinion, there appears to be a group of patients with considerable vasospasm who can be much benefited by lumbar procaine block of the sympathetic system and sympathectomy. The average age of these patients was sixty years; in all pulsation was absent in the posterior tibial and dorsalis pedis arteries, but gangrene of the feet had not supervened. Four of the seven patients had previously undergone medical treatment, and three had bilateral intermittent claudication. It is pointed out that patients with arteriosclerotic endarteritis have recently received less attention because the operative results have often been disappointing and the lesions have been regarded as end-results in which vasospasm does not occur (J. Homans); Ives contests these conclusions and quotes opinions on both sides, such as those of R. L. Harris who reported a good result in 42 per cent of twelve cases after sympathectomy.

Coarctation of the aorta

Adult type

Occurrence in children.—P. H. Rhodes and E. Durbin report three cases and collect statistics of forty-seven in which the adult type of coarctation of the aorta has been diagnosed in children under the age of fifteen years. The diagnosis should be made as early as possible, because then the prohibition of strenuous exercise may prolong the patient's life. The authors point out that when the routine estimation of arterial blood pressure is taken it is taken on one side only—on the right arm; this is as it should be because it avoids the occasional fallacy of a low blood pressure in the left arm.

Babkin, B. P., Armour, J. C., and Webster, D. R. (1943) *Canad. med. Ass. J.*, **48**, 1.

Fauteux, M. (1940) *Surg. Gynec. Obstet.*, **71**, 151.

Harris, R. L. (1935) *Brit. J. Surg.*, **23**, 414.

Holman, R. L. (1943) *Amer. J. Path.*, **19**, 147, 159.

Homans, J. (1939) *Circulatory Diseases of the Extremities*, New York.

Ives, H. R. (1943) *Proc. R. Soc. Med.*, **36**, 339.

Oppel, W. A. (1913) *Wratschebnaja Gaz.*, **40**, 1241.

Rhodes, P. H., and Durbin, E. (1942) *Amer. J. Dis. Child.*, **64**, 1073.

Rich, A. R., and Gregory, J. E. (1943) *Johns Hopk. Hosp. Bull.*, **72**, 65.

ARTHRITIS: ACUTE ARTHRITIS

See also B.E.M.P., Vol. II, p. 68; and Cumulative Supplement, Key Nos. 94–97.

Gonococcal arthritis

Aetiology

Incidence and clinical characteristics.—Opening a discussion on gonococcal arthritis and 'rheumatism' at a joint meeting of the Section of Physical Medicine of the Royal Society of Medicine and the Medical Society for the Study of Venereal Diseases, G. D. Kersley reported fifty cases of rheumatism associated with gonorrhoea which had occurred in the Forces. Four of the patients had suffered from rheumatic symptoms which flared up after they acquired gonorrhoea; in four other patients the onset of rheumatism coincided with a recurrence of discharge, negative to tests for gonococci, long after the original gonorrhoeal infection took place. The other patients had recent infections. The clinical picture of gonorrhoeal rheumatism is very varied. Fascial structures are often attacked; synovitis is common, and arthritis, monarticular or polyarticular, may occur. Conditions which are so often associated with gonorrhoeal rheumatism as to be suggestive in diagnosis are conjunctivitis and iritis, keratodermia and calcaneal periostitis. The complement fixation test is of limited value, since it

may remain positive for years after the initial gonorrhoeal infection and does not denote activity. The knees and ankles were, in the author's series, the joints that were oftenest involved, and next in frequency were the fascial affections, especially of the feet. In thirty-seven cases the average period during which patients remained in hospital was 3.8 months, and ten men had to be discharged from the Army. Fasciitis proved to be particularly resistant to treatment. Various methods of treatment were used, including sulphanilamide administration, fever therapy, ionization and different forms of physiotherapy. Hyperthermia appeared to be the most effective treatment, especially when combined with chemotherapy, but it has risks, and in the above series was responsible for one death. A. King had encountered sixty-one cases of metastatic gonococcal lesions among 2,719 cases of urethritis (1,784 gonococcal cases and 935 non-specific cases), a percentage incidence of just over 2. The fact that the gonococcus cannot always be found should not, in King's opinion, weigh against a diagnosis of gonorrhoea. Prostatic culture is the most accurate test, but the technique is exacting. Treatment by sulphonamides gave disappointing results. Hyperthermia brought about improvement in fifteen out of sixteen cases.

Kersley, G. D., and King, A. (1942) *Proc. R. Soc. Med.*, **35**, 653.

ARTHRITIS: RHEUMATOID ARTHRITIS

See also B.E.M.P., Vol. II, p. 74; and Cumulative Supplement, Key No. 98.

Aetiology

Colonic infection

Pseudomonas pyocyanea.—P. E. Fiset reports a case of a man, aged seventy-seven, who for ten years had suffered from chronic articular rheumatism. The tonsils, teeth, sinuses and ears were normal. Chronic appendicitis was suspected and six bacteriological examinations of the faeces showed that *Pseudomonas pyocyanea* was present in striking abundance; it was thought that the man had contracted the infection ten years previously when working at a sewage system, a favourite medium for the above infection. The blood showed a strongly positive agglutination reaction, and cure was achieved by the oral administration of an autovaccine prepared according to a special technique. The efficacy of the vaccine was proved by the considerably increased rise of the patient's serum agglutinins.

Pathology and prognosis

Morbid changes

Chronic arthritis in adults: 'Felty's syndrome'.—L. M. Lockie, S. Sanes and S. L. Vaughan record two cases in women, aged respectively fifty-three and sixty-four, of the syndrome described by A. R. Felty in 1924 showing (in adults) the association of various conditions, particularly splenomegaly, enlarged liver, neutrophilic leucopenia, loss of weight, secondary anaemia, enlargement of the lymphatic glands, pigmentation of the skin, slight fever and rheumatoid arthritis. It has been suggested by other workers that Felty's syndrome is merely a rare form of rheumatoid (atrophic) arthritis, and that it is allied to Still's disease and to A. Chauffard and F. Ramond's diseases which show a considerable resemblance to Felty's syndrome in adults. In the first case observed by Lockie, Sanes and Vaughan there was a chronic non-specific inflammatory reaction, the spleen and lymphatic glands at necropsy showing sinus endothelial hyperplasia, phagocytosis and infiltration by plasma cells and eosinophils. The liver was degenerated with swelling of the reticulo-endothelial cells, and there were similar changes in other parts. H. A. Singer and H. A. Levy (1936) believed that *Streptococcus viridans* was usually responsible for the syndrome but that there might be other causal bacteria. Splenectomy has been employed therapeutically, but probably with only temporary benefit.

Histology of nerve lesions.—H. A. Freund, G. Steiner, B. Leichtentritt and A. E. Price record their histological findings in the lesions of the peripheral nerves in chronic atrophic (rheumatoid) arthritis. The nerves were obtained at necropsies. In three out of five cases of chronic rheumatoid arthritis the lesion was specific in the peripheral nerves, namely a nodulous rheumatoid perineuritis, consisting of accumulations of lymphocytes and plasma cells in the perineurium; it should be regarded as an active inflammatory process, concomitant and parallel with other rheumatic pathological features occurring in chronic rheumatoid arthritis, such as rheumatic heart disease, subcutaneous nodules and synovial inflammation and proliferation. The two others of the five cases showed only a mild lymphocytic inflammation. Out of eighty-six control cases seven showed pathological changes in the peripheral nerves, two being examples of chronic atrophic (rheumatoid) arthritis, one with nodular rheumatoid perineuritis. At an earlier stage of the examination of the nervous system the brain and the spinal cord only were investigated, no specific or characteristic change being found.

A. H. Baggenstoss and E. F. Rosenberg review the post-mortem data relating to thirty patients suffering from rheumatoid arthritis. The ages of the patients at the time of death ranged from nine to eighty-one years. The chief findings were as follows. Rheumatic lesions of the heart were found in sixteen cases and lesions which may have been of rheumatic origin, namely calcific aortic stenosis and chronic pericarditis, in two. In six others non-rheumatic cardiac lesions were found. Only two of the thirty patients had given a history of rheumatic

fever. No pulmonary lesion was found which could be considered specific, but in eight cases pleural adhesions were present for which a cause was not apparent and which may have been rheumatic. Chronic hepatic congestion, present in eighteen cases, reflected the high incidence of heart disease. Central necrosis was observed in four cases and possibly resulted from the arthritis or from some remedy given for its relief. Fatty changes were present in the liver in seven cases and were possibly related to the arthritis. Slight general enlargement of the lymph glands and spleen with hyperplasia of the reticulo-endothelial cells occurred in some cases. Low-grade non-specific glomerulo-nephritis was found in nineteen instances.

Treatment

Medicinal

Chrysotherapy.—R. H. Freyberg of Ann Arbor reviews the results of the treatment of rheumatoid arthritis by gold salts. Although, with few exceptions, the workers who have had experience of the use of gold salts in rheumatoid arthritis have obtained better results from them than from other forms of treatment, the benefit has not been uniform, and the frequency and sometimes the severity of the toxic reactions have interfered with the use of gold compounds. A number of gold preparations have been used, both organic and inorganic, some soluble in water, others insoluble in water; some are given in solution, others in colloidal suspensions. Although aurothioglucose is soluble, it is prepared in suspension in oil as solganal B oleosum. The gold content of the available gold salts varies from 37 to 87 per cent, and their efficacy depends on their gold content and not on their content of sulphur or of other constituents; the manner of their action and their fate in the human body are largely unknown. Being convinced of the therapeutic value of gold salts in rheumatoid arthritis, Freyberg reports his observations on the metabolic changes caused by chrysotherapy. A highly accurate and sensitive chemical method, namely that devised by W. D. Block and O. H. Buchanan was used to determine the gold content of the blood and the excretion of gold that occurred during and after treatment. When increasing weekly doses of the soluble crystalline gold salt, sodium aurothiomalate, were given intramuscularly, there appeared a step-like increase in the plasma gold concentration, a change on which much emphasis is laid. Gold was found in the plasma and in the urine for many months after the last injection of sodium aurothiomalate had been given. The best method of treatment is by myocrysin which has a 50 per cent gold content, the substance used in America is myochrysine. Doses increasing from 10 to 100 milligrams ($\frac{1}{2}$ to 1½ grains) weekly should be injected until a total of 1 gramme (15 grains) has been given; toxic reactions do not usually appear until several hundred milligrams of the drug have been injected. At present there is not any therapeutically effective drug which is devoid of potential toxicity.

Calcium aurothiomalate is a new gold salt which is used for the treatment of rheumatoid arthritis. A. B. Sabin gives an account of his work on treatment by its use. In 1938 it was found that some stocks of mice carry in their upper respiratory tract a filtrable micro-organism of the pleuro-pneumonic group which, on intravenous injection, had an affinity which was almost confined to the joints, the condition caused by the organism resembled rheumatoid arthritis in human beings in many of its clinical and pathological features. Although many attempts to find a similar micro-organism in rheumatoid arthritis in human beings have failed, it was thought that the experimental disease in mice and the human type of disease might respond in the same way to a number of chemotherapeutic agents. Among 603 mice with established experimental arthritis which were treated by adequate doses of suitable gold compounds, 86 per cent were completely cured, but the cure occurred only when treatment was begun within three weeks of the onset of the disease. Although the therapeutic effect of gold salts depends on the gold content, it was found that their toxicity depends on the nature of the radical to which the gold is attached and on the solubility or relative insolubility of the compound. Tests with the one insoluble gold compound, calcium aurothioglucolate, which was at first available, showed that, although it was non-toxic in 100-milligram doses per mouse weighing 20 grammes, almost ten times as big a dose as that of the soluble compounds was required to produce a therapeutic effect.

Baggenstoss, A. H., and Rosenberg, E. F. (1943) *Arch. Path.*, **35**, 503.

Block, W. D., and Buchanan, O. H. (1940) *J. Biol. Chem.*, **136**, 379.

Chauffard, A., and Ramond, F. (1896) *Rev. Médecine*, **16**, 334.

Felty, A. R. (1924) *Johns Hopk. Hosp. Bull.*, **35**, 16.

Fiset, P. E. (1942) *Canad. med. Ass. J.*, **47**, 545.

Freund, H. A., Steiner, G., Leichtentritt, B., and Price, A. E. (1942) *Amer. J. Path.*, **18**, 865.

Freyberg, R. H. (1942) *Proc. Mayo Clin.*, **17**, 534.

Lockie, L. M., Sanes, S., and Vaughan, S. L. (1942) *Amer. J. clin. Path.*, **12**, 372.

Sabin, A. B. (1942) *Proc. Mayo Clin.*, **17**, 542.

Singer, H. A., and Levy, H. A. (1936) *Arch. intern. Med.*, **57**, 576.

ARTHRITIS: SPONDYLITIS

See also B.E.M.P., Vol. II, p. 105.

Osteoarthritis of the spine*Treatment*

Physiotherapy.—A. S. B. Bankart points out that the symptoms and signs of spinal arthritis are well known and not easily mistaken, but that when a patient with the same symptoms complains of pain in the course of the sciatic nerve, the diagnosis most often made is not that of spinal arthritis: the symptoms are attributed to the effect of an inflamed peripheral nerve on the muscles and ligaments of the back. It is not a mere coincidence that both spinal arthritis and sciatica are common in middle-aged and elderly persons, nor is it just a chance that younger patients with traumatic spinal arthritis may also suffer from sciatica. The majority of the patients with sciatica seen in orthopaedic practice have symptoms and signs of spinal arthritis, which is by far the most common cause of sciatica. Severe osteoarthritis of the spine may occur without sciatica, and there may not be any radiological evidence of spinal arthritis. Bankart thinks it probable that sciatica is always due to neuritis, but he does not agree that the long nerve fibres which run all the way from the spinal cord to the terminations of the great sciatic nerve can be irritated or inflamed in only one particular part of their course, the thigh. For many years he has treated spinal arthritis and sciatica by manipulations and thereafter radiant heat, massage and exercises, in the belief that the sciatica and the stiffness of the spine are caused by the same periarticular inflammatory reaction. In persistent or recurrent cases he has removed the corresponding lateral intervertebral joints.

Bankart, A. S. B. (1943) *Proc. R. Soc. Med.*, **36**, 329.

ARTHROPODS AND DISEASE

See also B.E.M.P., Vol. II, p. 120; and Cumulative Supplement, Key No. 103

Arthropods as transmitters of disease*Biological transmitters*

Tick paralysis.—K. H. Abbott reviews the subject of tick paralysis which occurs after the bites of various ticks, namely the genera *Dermacentor*, *Haemaphysalis*, *Ixodes* and possibly also *Boophilus*, *Rhipicephalus* and *Hyalomma*. It occurs in the United States of America, Canada, Australia, Cape Colony, Crete, Yugoslavia, and possibly in other European countries. It attacks infants and children most often, and colts, calves, dogs, cats, rabbits, sheep, pigs and grouse. The most outstanding features are an ascending paralysis of the Landry type. If the tick is removed before bulbar paralysis appears, recovery usually follows. Experimentally the disease can be produced at any time of the year, but in the northern hemisphere it naturally occurs between February and August. It was noticed in sheep in 1825 by Hovell, but it was described more fully in Australia in this century. In 1898 probably the earliest scientific record in human beings (in two infants) was reported. Female children are much more often attacked than males. The patients are often irritable for twelve* or twenty-four hours before the onset of the flaccid paralysis. On awakening the patient may or may not complain of pain or sensory changes, may be unable to walk or feed himself, the spread of the paralysis is rapid—a matter of hours—and bulbar paralysis is shown by dysphagia, dysarthria and lingual and facial paralysis. The reflexes, tendon and superficial, are absent. Irregular, choreiform movements may occur, temperature and pulse are little altered. The most important aspect of treatment is to think of tick paralysis in every case of flaccid paralysis; it is then a simple matter to look for ticks concealed in the scalp, ears, axillae, the breasts, groins and perineum, and to remove them immediately by gentle traction. Various methods have been used to remove the 'head parts', such as the application of kerosene, gasoline, oil, ether, chloroform, heat and even excision of the skin containing the tick.

Abbott, K. H. (1943) *Proc. Mayo Clin.*, **18**, 39.

ASTHMA

See also B.E.M.P., Vol. II, p. 179, and Cumulative Supplement, Key No. 110.

Aetiology*Non-specific factors*

Psychic factors.—A Leading Article in the *British Medical Journal* draws attention to the psychological aspects of asthma. It has been suggested that asthma may have a symbolic value, the paroxysm representing in some way the underlying conflict, or that the attack is the equivalent of a suppressed cry for sympathy. A. Hurst considers that the commonest psychological exciting cause in asthma is expectation. An asthmatic who has been accustomed to have attacks under certain conditions may continue to have them after the original allergic or reflex factors cease to operate. Annoyance, excitement and anxiety may bring on an attack. In children a frequent cause of ill temper is a strict diet. Parental anxiety influences the asthmatic child and accounts in many cases for the bad effect of the home. Parents must be taught that the first essential in dealing with an asthmatic child is to hide any anxiety that they may feel. Children should not be pampered and should lead as normal a life as possible. It is difficult to decide how far the asthma personality or diathesis is the result of over-protection by anxious parents. This factor shows remarkable variations, the bronchial system appearing at times to lose the over-excitability characteristic of asthma. Allergy operates as a cause of asthma only in an individual having the asthma diathesis. Skin tests are very dis-

appointing. They seldom reveal an allergen responsible for a patient's attacks which had not already been recognized by careful inquiry; they sometimes indicate sensitivity to an allergen with which the patient never comes in contact; and sometimes indicate insensitivity to an allergen to which the patient is known to be sensitive. Reflex causes are usually to be found in the respiratory tract, especially the nose. C. H. Rogerson emphasizes the deleterious effect of parental anxiety. The personality of the asthmatic child is a psychological expression of his abnormal physical sensitiveness and irritability. The asthmatic attack may be symbolic of the nature of a mental conflict, as when a feeling of choking follows thoughts of drowning; or a sign of the conflict, as palpitation may be a sign of anxiety, without symbolizing its nature. It may be the result of a conditioned reflex, or may be a means to avoid a difficulty or to gain an end. The most important function of the psychological factor in asthma is to render the organism more sensitive to the physical factors which produce the attack.

Treatment

Treatment of attacks

Use of nicotinic acid.—G. Melton has treated nineteen patients with asthma during the attack with nicotinic acid, in the hope of producing dilatation of the bronchioles; the drug was given in doses of 50 or 100 milligrams, mostly by the intravenous route. Sixteen patients showed distinct improvement. Control injections of sterile water gave some relief in seven cases but were usually much less effective than the nicotinic acid. In thirty cases the drug was given over long periods in doses of 50 or 100 milligrams orally twice or thrice daily; children received half these doses. In sixteen patients the frequency and the severity of the attacks were considerably reduced.

Hurst, A. (1943) *Brit. med. J.*, **1**, 403.

Leading Article (1943) *Brit. med. J.*, **1**, 416.

Melton, G. (1943) *Brit. med. J.*, **1**, 600.

Rogerson, C. H. (1943) *Brit. med. J.*, **1**, 406.

AVIATION

See also B.E.M.P., Vol II, p 239, and Cumulative Supplement, Key No 116

Physiology of aviation

Effects of flying on aviators

Methods of bodily adjustments—J. F. Fulton, Sterling professor of physiology in the University of Yale, in the Shattuck lecture in May 1942 at the Annual Meeting of the Massachusetts Medical Society reviewed, under the title 'Medicine and Air Supremacy', the practical application of physiological research to aviation. With the help of Dr. and Mrs. E. C. Hoff a bibliography of 6,000 items, of which less than half are from medical journals, has been prepared by Fulton for the Committee on Aviation. The performance of modern aircraft has now far outstripped the physiological limitations of the pilot. The newer combat planes can fly higher than is compatible with life, even when the fliers are breathing pure oxygen. They can perform manoeuvres causing centrifugal force of such intensity that blood tends to be drawn away from the brain, a condition that results in transient blindness (blacking-out) and unconsciousness. The range of modern four-engined bombers, some of which can remain for twenty-four hours in the air, has raised problems of the effects on pilots and crews of fatigue, severe stresses and strains from cold, psychological tension and loss of sleep. It is the responsibility of Medicine in its broadest sense including psychology, psychiatry, physiology, and special branches of clinical medicine to protect air crews from these and many other risks. The most important problem is to raise the aviation 'ceiling' by the adjustment of the body to anoxia, which involves fundamental physiological, biochemical and endocrine research. In the numerous changes in the body when the latter is exposed to low oxygen partial pressure, recent work has shown the importance of the hormone of the adrenal cortex. In animals exposed to anoxia the adrenal cortex shows hypertrophy with subsequent degeneration; anoxia also causes loss of weight in all the organs except the adrenal cortex and perhaps the kidneys. Over-fatigued pilots, especially those subjected to many high-altitude flights, present the early symptoms of Addison's disease. As the adrenal cortex is probably activated by the adrenocortical hormone of the anterior lobe of the pituitary gland, it is not surprising that chronically hypophysectomized rats have not any greater altitude tolerance than the adrenalectomized animals. A second practical subject is reviewed—the safety crashes. The impact of the body, especially of the head, with some solid part of the aircraft is generally the cause of death or of serious injury in even minor accidents. When the body or the head strikes something that yields, as when the flier is thrown through a fabric roof or the wind-shield, the victim generally escapes serious injury. The basic factors governing the degree of injury in such circumstances are to be found in De Haven's analysis of non-fatal suicidal leaps from high buildings; it is shown that the victim usually landed on the back or flat on the stomach, or more interesting, that a slight degree of cushioning of the head, as in landing in a garden plot instead of on a cement sidewalk, prevented concussion and serious injury of other parts. Among 'stunt' drivers a practical application of the principle of gradual deceleration has long been used by circus performers who deliberately drive a car at sixty miles an hour into a brick wall; their trade secret is to jump into the back seat of the car and to lie hard against the rear of the front seat, a hand or an elbow being placed between the

side of the head and the back of the front seat. D. Denny-Brown and W. S. Russell have approached the problem of experimental concussion in the reverse direction by analysis of the factors of acceleration rather than of deceleration. When the head of an animal is struck by a moving pendulum, concussion does not occur unless the head is free to move, free to be accelerated. If a head, hard against an anvil or a brick wall, is accidentally struck, a nasty fracture may result, but the subject is not rendered unconscious; for this an acceleration of the head in space is essential. In Denny-Brown's experiments, the rate of acceleration necessary to cause concussion was relatively high—a critical value of 46,000 feet per second, per second. The occurrence of ruptured intervertebral disks is common, but not often diagnosed in the military or flying services. When flying men are manoeuvring, acceleration eight or nine times the normal acceleration of gravity may be induced and may cause strain and rupture of the disks. One means of lessening the physiological effects of high acceleration is the assumption of a crouching posture, which brings the lower extremities nearer to the heart and thus diminishes the length of the hydrostatic column of blood subjected to acceleration. There is not any doubt that the assumption of such posture increases tolerance to high degrees of acceleration, but it also greatly increases the strain on the lumbar vertebrae, the annulus fibrosus and the pulposus nuclei between the vertebrae. One or more of the nuclei may rupture, herniate into the spinal canal and cause acute sciatic pain.

Denny-Brown, D., and Russell, W. S. (1941) *Brain*, **64**, 93.

Iulton, J. F. (1942) *New Engl. J. Med.*, **226**, 873.

BITES AND STINGS

See also B.E.M.P., Vol. II, p. 343.

Arthropoda

Insecta

Mosquito-borne diseases —R. Fowler and A. H. Baldwin discuss the military significance of malaria and other mosquito-borne diseases. In 1918 Allenby's campaign was waged in territory notorious for endemic malaria, and both opposing armies suffered greatly. But Allenby, wittingly or unwittingly, took advantage of the fact that his medical services were the better and, by pinning the enemy to a line infested by *Anopheles* mosquitoes for nearly a year, reduced him to a condition in which the final assault made him an easy prey. Today the situation in the Pacific Ocean lends enormous strategic importance to the Panama Canal and the Singapore base. Neither would have been inhabitable by whites without the conquest of mosquito-borne disease. The prevention of malaria among armies in the field requires the provision of mobile laboratories and the use of quinine which, although not a cure, keeps the parasites out of the blood stream, thus preventing the development of symptoms. Mosquito-net discipline and anti-mosquito measures are difficult to carry out under war conditions. Dengue is another mosquito-borne disease which may suspend military operations completely for two or three weeks, since it spreads so rapidly that three-quarters of a force may be incapacitated simultaneously. Yellow fever is also a menace to armies in infected regions.

Fowler, R., and Baldwin, A. H. (1942) *Med. J. Aust.*, **2**, 455

BLADDER DISEASES

See also B.E.M.P., Vol. II, p. 374; and Cumulative Supplement, Key Nos. 136-146

Neoplasms

Vesical papilloma

Treatment of papillomatosis by disinfectants —T. J. Kirwin postulates the theory that papillomatosis of the bladder is caused by a virus. Papillomas of the bladder have much in common with warts of the skin of which the infective origin has been demonstrated. The empty bladder lies in apposed folds and thus presents favourable conditions for contact infection. Acting upon the above hypothesis the author treats vesical papillomas by opening the bladder and excising the growths with the diathermy knife. He then applies 50 per cent phenol to the entire bladder cavity so as to disinfect the mucosa. Four cases have been treated, but details are not given.

Diverticulum

Treatment

By operation and the use of sodium chloride. The combined use of surgery and sclerosing solutions in the treatment of large, inaccessible diverticula of the bladder is recommended by J. J. Bottone and F. L. Senger, who point out that excision of such diverticula may be difficult and hazardous. The presence of infection may lead to the formation of dense adhesions to important structures and prevent complete mobilization of the sac. Shock, haemorrhage and pericystitis contribute to a high operative mortality. The authors have tried the above method in one case, that of a debilitated man of sixty-nine with an inaccessible, very large, non-draining diverticulum causing pyuria, haematuria and pain on micturition. Seven months before, a two-stage prostatectomy had been performed. At operation the diverticulum could not be mobilized owing to dense adhesions. The bladder was opened and the mouth of the diverticulum found. It was separated from the bladder and the latter repaired and drained. The diverticulum also was closed about a self-retaining catheter. Two separate sacs were thus

formed. The diverticulum was irrigated until the infection had been overcome and then a 30 per cent sodium chloride solution was introduced through the tube, left for two hours and drained off. This was done twice a week until the mucosa was believed to have been destroyed. The catheter was then removed and the cavity allowed to close. No local or general reaction occurred throughout. The patient was discharged with a suprapubic cystostomy. He subsequently improved so much that the cystostomy opening could be allowed to close.

Bottomone, J. J., and Senger, F. L. (1943) *Urol. cutan. Rev.*, **47**, 79.

Kirwin, T. J. (1943) *J. Urol.*, **49**, 1.

BLASTOMYCOSIS

See also B.E.M.P., Vol. II, p. 403.

Coccidioidal granuloma

Clinical picture

Valley fever and coccidioidal granuloma.—G. W. Stiles and C. L. Davis have reviewed the subject of coccidioidal infection in man and animals. In human beings, infection by *Coccidioides immitis* occurs either as an acute non-fatal disease (also known as valley fever) or as a chronic, often fatal affection, coccidioidal granuloma. Valley fever resembles influenza, sometimes accompanied by an erythematous rash; the mortality is negligible. Coccidioidal granuloma may affect any part of the body, but in the majority of cases the initial lesion appears to be in the lung; the mortality in a series of 744 cases was 40 per cent. The pulmonary form closely resembles tuberculosis, but the fungus may be found in the sputum; when lesions occur in other organs biopsy is required for diagnosis. Infection probably takes place by the inhalation of spore-laden dust, rarely through an abrasion of the skin or through the gastrointestinal tract. Among animals coccidioidal infection is not uncommon. It has been observed in cattle, trapped rodents (of 125 carcasses in one series, 25 were infected), dogs and sheep; the excreta of such animals may be a source of soil contamination. The disease, both in man and in animals, has been observed mainly in California but cases have recently occurred in other localities and it is possibly becoming more widespread.

Stiles, G. W., and Davis, C. L. (1942) *J. Amer. med. Ass.*, **119**, 765.

BLINDNESS

See also B.E.M.P., Vol. II, p. 407; and Cumulative Supplement, Key Nos. 149–162.

Definition and classification

Classification

Causes and incidence.—Material gathered during more than ten years' work by the Regional Clinic for Certification of the Blind, Glasgow and South-West Scotland, is analysed by J. Marshall and H. E. Seiler in a report of which both parts have now been published. The Clinic was established in order that persons seeking enrolment on the Register of the Blind should be examined by a panel of ophthalmologists. Three groups are distinguished as follows. (1) persons with visual acuity of less than three-sixtieths Snellen, who are counted as blind; (2) persons with visual acuity of six-sixtieths or better, who are not counted as blind unless the field of vision is contracted to ten degrees or less throughout the greater part of its extent; (3) persons with intermediate degrees of visual acuity, that is, between three-sixtieths and six-sixtieths, who are regarded as blind (a) if aphakic or (b) if the visual field is restricted. The population served by the Clinic totals 2,578,709 persons. The number of patients who have been examined is 3,219, including 1,734 males and 1,485 females. More than half the patients were aged over fifty when they became blind but, in nearly two-thirds, the condition causing blindness had arisen before that age, and in 36.66 per cent it had arisen by the age of fifteen. The causes fall into five categories: (1) Congenital and undetermined conditions; (2) infectious or toxic conditions, (a) exogenous, (b) endogenous; (3) traumatic and chemotoxic conditions; (4) general diseases; (5) unclassified. The six most important causes were cataract, myopia, glaucoma, chronic septicaemia, venereal disease and injury, which between them all accounted for three-quarters of the cases. Ophthalmia neonatorum caused blindness in 3.07 per cent, and in all cases both eyes were affected. Restoration of vision was considered possible in only three cases. Syphilis accounted for 348 cases (10.81 per cent), and of these 152 were due to congenital syphilis. The incidence in males is significantly higher in all the main groups. Miners show a much higher incidence than does any other occupational group. The rate of blindness among Irish people is significantly in excess of that for other nationalities as a whole.

Causes and treatment.—In the second part of their analysis, Marshall and Seiler record further important causes of blindness were chronic septicaemia and trauma. The diagnosis of septicaemia included a number of cases of unknown aetiology; all cases thus classified have in common an inflammatory reaction in the tissues of the eye; this group comprised 10.72 per cent of all the cases. Injury alone was responsible for blindness in 5.22 per cent and, in conjunction with other causes, for a further 6.15 per cent; industrial accidents accounted for a large proportion (48.09 per cent) of the 366 cases in which injury, alone or combined with other factors, had resulted in blindness; two-thirds of the patients were

employed either in the mining and quarrying or in the metal industries, and the former group included twice as many cases as the latter. Diabetes mellitus caused blindness in 1·3 per cent of the patients, all of whom were binocularly affected and 81 per cent were women. The eye defects most commonly seen were cataract and aphakia, myopia, optic atrophy, corneal ulcer, primary glaucoma and irido-cyclitis, which together accounted for 72·9 per cent of the cases. As regards prevention of blindness, eugenic sterilization is not considered to be either practicable or worth while; medical treatment may be of some use in congenital syphilis and ophthalmia neonatorum; protective devices in industry might be of considerable value. Treatment may restore useful vision in a number of patients; of those in the present series who underwent surgical treatment, 56 per cent were subsequently removed from the 'blind' category. Many patients were unwilling to submit to treatment, and it is noted in this connexion that in many countries pensions for blindness are given only to the 'incurable blind'.

Congenital defects

Choroid, retina and iris

Night-blindness.—The importance of night vision in the Forces is emphasized in an address by W. J. Hope-Robertson to the Wellington division of the British Medical Association. In many service jobs good night-vision is essential and every medical officer ought to possess some knowledge of the subject. Special tests of night visual capacity are carried out in all branches of the Royal Air Force and the Royal New Zealand Air Force, and rough estimates are made in the Navy and certain branches of the Army. Civilians, especially those who drive cars, also require good night-vision. Since night visual capacity decreases rapidly after the age of forty-five years, many elderly people are quite unfit to drive cars after dark. The power of dark-adaptation depends in some way upon the retinal pigments rhodopsin and the recently discovered iodopsin. Rhodopsin is closely related to vitamin A and is partially converted into this substance by prolonged exposure to light. The parts played respectively by the pigments and by the rods and cones of the retina in dark-adaptation are at present unknown, but it is known that the rods are much more responsible than are the cones. A number of diseases of the eye will interfere with dark-adaptation, which also varies between one normal person and another. The larger the pupil, for instance, the greater is the night visual capacity, and experiments in dilatation of the pupil have been carried out on aviators. Deficiency of vitamin A produces night-blindness, and since the time of Hippocrates raw liver has been recommended as a cure. Vitamin C may also have some connexion with dark-adaptation. Lowering of general health, fatigue and lack of oxygen have a deleterious effect on dark-adaptation. Psychological factors are of great importance and officers in the Forces are advised to prevent their men from believing that night-blindness is a common disease.

Trauma

Perforating wounds

Prevention and treatment of injuries by steel particles.—F. D. Gulliver has observed that the majority of steel particles which penetrate the eye-ball originate from the mushroomed heads of cold steel hammers, drills or chisels. He estimates that if mechanics could be taught to realize the danger of using defective tools, the number of intra-ocular foreign bodies would be reduced by at least 50 per cent. The employer or shop foreman should inspect hammers and chisels daily to see that all overhanging edges have been ground off. The employer should insist on protective goggles being worn by all workmen who are exposed to the risk of foreign bodies entering the eyes. In the author's series of 1,800 cases, in 80 per cent the wound of entrance was through the cornea, and in 85 per cent the foreign body lay in the posterior chamber; the shape and size of the particle varied greatly. Particles measuring not more than 0·5 millimetre are difficult to show in a radiograph, which should be taken in every case in which the history suggests the possibility of an intra-ocular foreign body, including any case of acute inflammation of the eye occurring after the use of a hammer and chisel. The patient is sometimes unaware that a particle has entered the eye. It is essential that the radiologist should be specially trained in this type of work. Removal of the particle should be carried out by the anterior route except in cases in which the wound of entrance is in the sclera and is sufficiently large to warrant an attempt to withdraw the foreign body through it; or in which the foreign body is caught either in the choroid or sclera or in an inflammatory exudate and cannot be drawn by the giant magnet into the anterior chamber. The results of removal are good, normal or little less than normal vision being retained in 80 to 90 per cent of cases.

Gulliver, F. D. (1942) *Arch. Ophthalm.*, N.Y., **28**, 896.

Hope-Robertson, W. J. (1942) *N.Z. med. J.*, **41**, 159.

Marshall, J., and Seiler, H. E. (1942) *Brit. J. Ophthalm.*, **26**, 337.

— — (1942) *ibid.*, **26**, 385.

BLOOD EXAMINATION

See also B.E.M.P., Vol. II, p. 457; and Cumulative Supplement, Key Nos. 163–169.

Cellular changes (blood count)

Haemoglobin determination

In women and children.—Helen M. M. Mackay, R. H. Dobbs, Lucy Wills and Kaitilin Bingham have estimated the haemoglobin in 1,074 women and children. The subjects were

divided into four groups comprised as follows. (1) 364 persons aged from six months to five years; (2) 128, aged from five to fifteen years; (3) thirty-eight (factory girls), aged from fourteen to eighteen years; (4) women of eighteen upwards—(a) 353 nurses and students, (b) 159 factory hands, (c) thirty-two housewives. In all but two of the groups the haemoglobin values were disquietingly low. In group (1) the average was 76.6 per cent; the highest levels were found in children living at home and attending welfare centres, the lowest in children in residential nurseries. In group (2) the average was 84.5. In group (3), consisting of workers in a factory in a small town near London, it was much higher (98 per cent). Group 4(a) was subdivided into London and country dwellers; the respective averages were 90.6 and 84.1. The country dwellers were living in billets and were very badly fed. In group 4(b), consisting of workers in a small town, in the same factory as those in group 3, the average was 94 per cent. In group 4(c) the average was 89.6. The importance of counteracting the deficient iron intake shown by this investigation is emphasized.

Coagulation (blood platelets)

Platelet count

Effects of heparin in normal and in haemophilic blood.—A. L. Copley and T. P. Robb report on further work on blood platelets. In fourteen out of fifteen dogs which received a single intravenous injection of heparin the platelet count fell within five minutes. In 1916 G. R. Minot and R. L. Lee described haemophilic platelets as being more resistant to lysis, and accordingly Copley and Robb tested the sensitivity of two cases of haemophilic blood to heparin, and report that no decrease of the platelet count was due to heparin.

Serological tests

Haemagglutination (blood grouping)

Racial incidence of the Rhesus factor.—The distribution of the individual blood properties in American Indians has been investigated by K. Landsteiner, A. S. Wiener and G. A. Matson, with special reference to the Rh factor. The results showed a striking difference between Indians and the white population of New York City; in the latter the percentage of Rh positive individuals was 85.3, whereas among 120 full-blooded Indians only one Rh negative individual was found, making the percentage of Rh positives 99.2. In Indians not of pure blood the distribution of the factor was intermediate between that found in whites and in pure Indians respectively. A variant of Rh, demonstrable by a special serum giving about 27 per cent of negatives in whites, was more than twice as frequent in full-blooded Indians as in whites. Tests for other blood properties confirmed the findings of other workers, namely high frequency of group O, low frequency of type N

Physical and chemical changes

Sedimentation of red cells

Value in prognosis.—L. Lewis-Fanning and M. Myers have studied the blood sedimentation rate in sanatorium patients with a view to determining the prognostic value of the test. Estimations were made on admission and discharge with regard to every patient admitted during the three years 1936 to 1939. Patients who died in the sanatorium are excluded. Six hundred and thirty patients, 292 males and 338 females, were included in the survey. The patients were kept constantly under observation until the end of April 1940, so that none was observed for more than forty-two months. Deaths during this period of observation were as follows: B.S.R. under four on discharge (135 patients), no deaths; B.S.R. five to nine (161 patients), no deaths in males, two deaths in females; B.S.R. ten to twenty-nine (236 patients), nine deaths in males and five in females; B.S.R. thirty to forty-nine (fifty-nine patients), seven deaths in males and five in females; B.S.R. fifty and over (thirty-nine patients), nine deaths in males and two in females. The figures show, in the males, a clear association between the B.S.R. on discharge and the subsequent course of the disease, in the females the association is less distinct, although probable. Further analysis of the different groups of patients indicated that the average prognosis is worse when the B.S.R. is high on admission and does not rise or fall notably during treatment.

Miscellaneous

Haemoglobin derivatives

Cerebral anoxia.—Signs and symptoms of cerebral anoxia, associated with a fall in oxygen saturation, occur at a height of over 35,000 feet, even when the subject breathes pure oxygen. Studies have been made by H. Himwich, J. Fazekas, H. Herrlich, A. E. Johnson and A. L. Barach on five dogs and three normal human subjects to ascertain whether or not the addition of carbon dioxide to oxygen-enriched atmospheres makes any difference to the composition either of arterial blood, or of the venous blood returning from the brain, as compared with mixed venous blood. Venous blood from the brain was obtained in dogs by trephining the skull and using the superior longitudinal sinus; in the human subjects it was obtained from the internal jugular vein. Arterial blood was also examined. The equivalent at sea level of 2 per cent of carbon dioxide in oxygen was administered by means of a mask at a pressure corresponding to an altitude of 38,000 feet. No evidence was obtained that the carbon dioxide-oxygen mixture presented any advantages over pure oxygen in its effect upon cerebral oxygen tension. The average fall in oxygen saturation of the cerebral venous blood after exposure to a simulated height of 38,000 feet was approximately the same, whether the

subject breathed pure oxygen or the mixture. Blood oxygen levels showed differences which in all instances were extremely small and did not show any uniformity of direction.

Copley, A. L., and Robb, T. P. (1942) *Amer. J. clin. Path.*, **12**, 416.

Himwich, H., Fazekas, J., Herrlich, H., Johnson, A. E., and Barach, A. L. (1942) *J. Aviat. Med.*, **13**, 177.

Landsteiner, K., Wiener, A. S., and Matson, G. A. (1942) *J. exp. Med.*, **76**, 73.

Lewis-Fanning, E., and Myers, M. (1942) *Brit. med. J.*, **2**, 125.

Mackay, Helen M. M., Dobbs, R. H., Wills, Lucy, and Bingham, Kaitilin (1942) *Lancet*, **2**, 32.

Minot, G. R., and Lee, R. L. (1916) *Arch. intern. Med.*, **18**, 474.

BLOOD PRESSURE, HIGH AND LOW

See also B.E.M.P., Vol. II, p. 503; and Cumulative Supplement, Key Nos. 170 and 171.

High blood pressure

Essential hypertension

Aetiology.—R. W. Scott, addressing the Section on Practice of Medicine of the American Medical Association, discussed the aetiology and pathogenesis of arterial hypertension in the light of recent experimental research. Setting aside the occasional case in which hypertension results from endocrine disorders such as dysfunction or tumours of the pituitary or adrenal glands, or from disorders of the nervous system, he states that the majority of patients do not show any evidence of disease of the endocrine organs, unless the kidney be regarded as belonging to the latter category. The author's thesis is that arterial and arteriolar sclerosis of the kidney vessels excites a renal humoral mechanism which produces increased tone in the peripheral arterioles and thus raises the systemic blood pressure. Evidence is cited to show that a direct relation exists between disease of the kidney and the peripheral vascular tone. In the condition of so-called essential hypertension, in which the patient does not at any time develop clinical signs of renal disease or of general arteriosclerosis, the rise of blood pressure is produced by general vasoconstriction; but observations by F. Volhard and K. T. Fahr have shown that the kidney in such cases exhibits more or less widespread sclerosis of the smaller arteries, a condition which they termed nephrosclerosis. Although patients with essential hypertension may not show any signs of renal disease during life, a sufficiently careful search at necropsy shows sclerosis of the intrarenal arteries in practically every case. The phenomena of malignant hypertension can be reproduced in animals by interference with the renal blood supply outside the kidney, and in many cases of clinical hypertension significant sclerosis of the main renal arteries has been discovered at necropsy. Unilateral renal disease may be associated with elevation of blood pressure, and the removal of the affected kidney with a return to normal conditions. The author maintains that the type of hypertension, benign or malignant, which results from nephrosclerosis depends upon the extent and progress of the vascular lesions in the kidney.

Treatment by sympathectomy.—J. Bordley, III, M. Galdston and W. E. Dandy report the results of sympathectomy for essential hypertension in ten patients observed for periods of from three to seven years after the operation. As the authors say, most of the previously published cases have not been watched for a sufficient length of time. The ten patients described were survivors of a group of twelve operated upon, three by the supradiaphragmatic and nine by the infradiaphragmatic route. Two died shortly after operation. All were suffering from incapacitating symptoms. Thorough investigation was carried out in hospital prior to operation, and the completeness of the sympathetic interruption was checked after operation by starch-iodine sweating tests and other procedures, which were repeated at intervals in order to detect any evidence of sympathetic regeneration in patients subjected to infradiaphragmatic sympathectomy. The results observed were as follows. Nine of the patients were relieved of their symptoms after the operation; in five the arterial pressure was lowered; the others did not show any change of pressure. In four of the five patients whose blood pressure fell the latter subsequently rose again to pre-operative levels and the symptoms returned. The fifth patient's pressure returned to its former level in under two years and objective signs of cardiovascular renal disease have increased, but he has remained free from symptoms for four years. The level of arterial pressure was lowered for periods of from six to eighteen months in four of the nine patients treated by infradiaphragmatic sympathectomy and for four and one-half years in one of the three treated by supradiaphragmatic sympathectomy. During the period of lowered pressure two patients showed regression of abnormal physical signs, but renewed progression occurred as the pressure rose again. Return of the arterial pressure to its pre-operative level was not associated with evidence of sympathetic regeneration. No correlation was observed between the effect of operation on the blood pressure and the pre-operative response to sodium amytal. Postural hypotension, lasting from six to nine months, occurred in four patients, all operated upon by the infradiaphragmatic route. In three instances it was accompanied by postural dyspnoea. There was not any alteration of sexual function after infradiaphragmatic sympathectomy.

Course and prognosis

What is the normal blood pressure?—In a paper read before the American Medical Association R. M. Daley, H. E. Ungerleider and R. S. Gubner consider the prognosis in hyper-

tension. The latter condition is important for two reasons: as an indication of underlying disease, and because of the effects of the high pressure as such. Hypertension may result from renal, endocrine or vascular lesions, disease of the central nervous system or, in the type known as essential hypertension, from causes still unknown. Cases of unknown aetiology constitute the great majority. In considering hypertension the first requisite is a standard of normal pressure. The present tendency is to set the normal at a lower level and to regard 140 systolic and 90 diastolic as the upper limits of normality. A study made in 1939 by a committee representing life insurance medical officers in America demonstrated conclusively that the actual mortality exceeds the expected mortality in a rapidly rising ratio for blood pressures above this level. Blood pressures below the average carry an improved expectation of life. The blood pressure tends to vary widely at first but with the development of organic changes in the vessels it becomes more constant. The fall of pressure resulting from inhalation of amyl nitrite has been proposed as a prognostic test in hypertension. Other methods of discovering the extent of vascular degeneration are pectoral muscle biopsy and retinoscopy. The data thus obtained are, however, of less prognostic value than are those of the cardiac and coronary changes which depend more upon the duration than the degree of the hypertension, and which are best estimated by electrocardiography and radiography. Examination of the urine has little prognostic value. Heredity, age of onset, physical build and sex are all of importance in prognosis. Treatment in early cases may improve the outlook but can have little effect once organic changes have occurred.

High blood pressure in general

Aetiology

Goormaghtigh cells.—W. Kaufmann reports his observations on approximately 400 human kidneys obtained at necropsy or at operation on patients with and without hypertension, regarding the presence of cells at the vascular pole of the renal glomeruli in the outer part of the cortex. These cells are called by Kaufmann 'Goormaghtigh cells' (after N. Goormaghtigh, who has described them on several occasions since 1932 and who in 1939 suggested that the cells, which are present normally, underwent hyperplasia and exerted an endocrine hypertensive effect). Among Kaufmann's cases, which ranged from a male infant aged three months to a woman aged seventy-eight years, were many examples of benign progressive arteriolar nephrosclerosis. From recent observations it seems justifiable to add to the known structures of the normal human nephron two others which are constantly present in the renal cortex, they are the Goormaghtigh cells of the arteriolar walls and the macula densa of the distal convoluted tubules. The article is illustrated by six plates and among the fifty references there are six to Goormaghtigh.

Intrarenal pelvis.—It has been suggested that when the renal pelvis lies wholly within the substance of the kidney it may exercise pressure upon the renal vessels and be a predisposing factor in hyperpiesia. A. Hyman and N. C. Schlossman have examined fifty-five subjects at necropsy with special regard to this point. All had suffered from hyperpiesia during life. It was found that the incidence of intrarenal and of extrarenal pelvis was roughly equal. The authors also compared 200 excretory pyelograms with the blood pressures of the patients concerned. Of the patients with an intrarenal pelvis, hyperpiesia was present in 31·2 per cent, and of those with an extrarenal pelvis it was present in 26·0 per cent. In a group of cases of hydronephrosis, on the other hand, hyperpiesia accompanied an extrarenal pelvis in 26·6 per cent and an intrarenal pelvis in 8·7 per cent of the patients. In forty-three cases of nephroptosis the proportion of high pressures was the same with both types of pelvis. Rats, in which the pelvis is intrarenal, when kept in an upright position for two weeks did not show any change in blood pressure despite the descent of the kidney and consequent hypothetical kinking of the pelvis or ureter.

Vitamin B deficiency.—R. M. Calder has studied the effects of vitamin B deficiencies upon the blood pressure of rats, in the hope of throwing light upon the origin of hypertension in human beings. The rats, bred especially for the experiment, varied in age from eight to ten weeks. A group of fifty rats was placed on a basic diet free from all components of the vitamin B complex; after two weeks thiamine hydrochloride was administered. During the first week the animals showed a slight but significant rise in the average blood pressure; by the end of the second week, however, the average reading had fallen slightly below the initial level. With the addition of thiamine hydrochloride the average pressure rose immediately and, by the end of the fifth week, was still significantly high. By this time the animals had begun to show signs of gross riboflavin deficiency and six had died. A second group of fifty rats, intended to serve as a control, received the same diet as the first group together with 5 per cent of autoclaved yeast; this proved insufficient to prevent a rise of blood pressure, and at the end of two weeks the percentage of yeast was increased to 10. During the third week the blood pressure dropped, but did not reach its original level until a further addition of liver extract or extract of rice polishings had been made. The effects of partial deficiencies of vitamin B complex were tested on five groups of twenty-five rats. All received the basic diet, with the addition of thiamine. Supplementary feeding was as follows. Group 1, liver extract; group 2, none; group 3, autoclaved yeast, 2·5 per cent of the weight of the food given; group 4, 5 per cent yeast; group 5, yeast to any amount. Group 1 (control) did not show any variation from the normal blood pressure readings. In all the other groups blood pressures rose, even

in group 5, in which vitamin B intake should have been adequate; the animals in this group at first refused to eat enough yeast and, when they took more, blood pressures tended to drop. Partial deficiencies caused a greater rise of pressure than complete deficiencies, possibly because of the debilitating effects of the latter. It was found that when the total diet was deficient a rise of blood pressure took place even with excessive intake of vitamin B₂.

Bordley, J., III, Galdston, M., and Dandy, W. E. (1943) *Johns Hopk. Hosp. Bull.*, **72**, 127.

Calder, R. M. (1942) *J. exp. Med.*, **76**, 1.

Daley, R. M., Ungerleider, H. E., and Gubner, R. S. (1943) *J. Amer. med. Ass.*, **121**, 383.

Goormaghtigh, N. (1932) *Arch. Biol., Paris*, **43**, 575.

— (1939) *Brux. Méd.*, **19**, 1541.

Hyman, A., and Schlossman, N. C. (1942) *J. Urol.*, **48**, 1.

Kaufmann, W. (1942) *Amer. J. Path.*, **18**, 783.

Scott, R. W. (1942) *J. Amer. med. Ass.*, **120**, 1.

Volhard, F., and Fahr, K. T. (1914) *Die Brightsche Nierenkrankheit, Klinik, Pathologie und Atlas*, Berlin.

BLOOD TRANSFUSION

See also B.E.M.P., Vol. II, p 530, and Cumulative Supplement, Key No 172.

Technique of transfusion

Gelatin

Gelatin solutions.—Experiments in the use of autoclaved gelatin solutions of varying concentrations for transfusion are described by H. Gordon, L. J. Hoge and H. Lawson. A preliminary study of the toxicity of the solutions was made by experiments on forty-five dogs, and ill effects were not observed either during life or *post mortem*, nor was evidence obtained of sensitization. A comparison was then made of the power of gelatin solutions, glucose saline and defibrinated blood to restore the circulation after massive haemorrhage. Determinations of the percentage elevation of arterial pressure, the length of time (up to two hours) that the level was maintained and the ability of the animal to stand a second haemorrhage, were made by withdrawing known amounts of blood from anaesthetized dogs until the blood pressure had fallen to a critical level and by immediately injecting an equal quantity of the solution to be tested. It was found that all three solutions produced practically complete immediate restoration of normal arterial blood pressure. With defibrinated blood restoration remained almost complete at two hours; with gelatin it was about 86 per cent complete, whereas with glucose-saline it was only 62 per cent complete after thirty minutes. The fall of pressure during a second bleeding was not any greater after the use of gelatin than after defibrinated blood, and was considerably less than after glucose-saline. Gelatin may therefore be of considerable value in many clinical emergencies.

Gordon, H., Hoge, L. J., and Lawson, H. (1942) *Amer. J. med. Sci.*, **204**, 4.

BONE DISEASES

See also B.E.M.P., Vol. II, p 553; and Cumulative Supplement, Key Nos. 175–184.

Congenital bone dystrophies, generalized

Dyschondroplasia (multiple chondromas)

Maffucci's syndrome.—Alice Carleton, J. St. C. Elkington, J. G. Greenfield and A. H. T. Robb-Smith report two cases and collect eighteen previously recorded examples of a syndrome consisting of the combination of dyschondroplasia (Ollier's disease) and vascular hamartomas (cavernous angiomas), which they call Maffucci's syndrome after the man who first described it in 1881. There are four additional cases which may be regarded as '*formes frustes*'. Dyschondroplasia, described and named by L. Ollier in 1900, may have been regarded in earlier papers as being congenital rickets. In a typical case of the syndrome the child—who is born normal—is usually a male between the ages of one and twelve years, and is found to have a hard nodule from one to two centimetres in diameter, occurring most often on a finger or toe; other lesions soon appear involving the extremities and limbs, either unilaterally or extremely asymmetrically. Dilated veins and soft bluish tumours appear, and fracture of one or more bones may follow a trivial injury; one or more of the long bones has a short shaft with expanded ends, and may show cartilaginous tumours which occur especially near the epiphysial line. Throughout the period of development the deformities increase, and the hands and feet become almost unrecognizable and are transformed into huge tumour masses. When growth comes to an end the syndrome becomes stationary, but injury may be followed by a recrudescence; malignant changes have been recorded. Analysis of the cases suggests that the two components of the syndrome have a coincidental association and that the vascular anomalies do not induce the bone changes, but it is possible that both are the result of a foetal neurotrophic disturbance.

Polyostotic fibrous dysplasia (Albright's syndrome)

Clinical picture.—M. A. Falconer and C. L. Cope record two cases, in a girl aged eighteen and in a boy aged ten, and have collected twenty-five similar reported examples of a com-

plicated clinical picture. This comprises fibrous dysplasia of bone (not of parathyroid gland origin), with cutaneous pigmentation and various endocrine disorders such as hyperthyroidism, acromegaly, and skeletal and sexual precocity. The recorded twenty-seven cases are analysed and show considerable variations. In 1937 F. Albright, A. M. Butler, A. O. Hampton and P. Smith reported five similar cases and collected fourteen others. In 1938 L. Lichtenstein described the bone lesion as polyostotic fibrous dysplasia, a subject on the histology of which A. H. T. Robb-Smith contributes a note to Falconer and Cope's paper. The disease is one of childhood and appears to be self-limiting since the active phase probably ends with the premature fusion of the epiphyses; it is not fatal. The bone changes may occur with or without endocrine disturbances or cutaneous pigmentation. The pathogenesis is not known but it is suggested that the disease is the result of a congenital disorder of development which involves both the bony skeleton and the hypothalamus. There is not any evidence that the condition is hereditary.

Tumours of bone

Non-malignant

Benign chondroblastoma.—H. L. Jaffe and L. Lichtenstein describe under the above title a tumour usually regarded as a variant of a giant-celled tumour (calcifying or chondromatous), and sometimes even as a malignant tumour of bone and specifically a chondrosarcoma or an osteogenic sarcoma. The lesion is, however, entirely benign and heals without recurrence after thorough curettage and even without supplementary irradiation. It arises from the epiphyses, but not as some have thought especially from the upper end of the humerus. It is not, however, a simple chondroma; the basic tumour cell is a round or polyhedral cell of moderate size with a large nucleus. Clumps of large multinuclear giant cells may occur in haemorrhagic areas around the vascular sinuses and even in the hyaline chondroid tissue.

Meloiheostosis.—Emily L. Franklin and I. Matheson record a case in a spinster, aged forty-one, of this rare bone disease. When the patient was ten years old the right lower limb was longer than the left and an operation, apparently a plantar fasciotomy to overcome an acquired cavus deformity, had been performed. 1 or from ten to fifteen years previous to June, 1941, at which time she came to hospital, she had been prone to attacks of ulceration of the dorsum of the right foot. The circumference of the right lower extremity, even when oedema had subsided, was about two inches longer than that of the left. There was a large bony boss on the right side of the skull, about four inches in diameter and raised about one inch above the normal part of the skull; the mass was attached to the right parietal and temporal bones; there was also bony enlargement of the right half of the body of the mandible, and the right ulna was irregularly enlarged. Radiologically, changes characteristic of meloiheostosis were present in many of the bones of the right side of the body and, except for the fifth lumbar vertebra, all the bones of the left side were normal. Apart from the bony changes there were some very dense nodular deposits in the soft tissues round the inner side of the lower end of the right femur and of the right ankle. The condition was described in 1922 by A. Léri and Joanny, and represents a hyperostosis of ivory-like bone of the bony cortex; it resembles the appearance of *coulée de bougie*, or molten wax streaming down one side of a candle. The original describers embody in their name meloiheostosis (μέλος, a limb, πέω, I flow) the picture of an excess of bone poured down one aspect of the bone; the present authors have collected and analysed thirty-eight reported cases. Of thirty cases nineteen were in males and eleven in females. The age at onset ranged up to forty-nine years; the upper limb was involved in eighteen cases and the lower limb in nineteen cases. Histological examinations were made in five cases. Léri and his co-workers suggested infection as a cause, V. Putti incriminated the vasomotor mechanism of the nutrient artery, and J. J. Moore and A. A. De Lormier suggested that the condition was due to subperiosteal telangiectasis with repeated petechial haemorrhages.

Malignant

Multiple myeloma.—L. Morissette and C. H. Watkins report on the findings of the blood smears in a hundred patients with probable or possible multiple myeloma. Of these, fifty-six were probably multiple myeloma as indicated by clinical and laboratory data. The significant blood findings in these fifty-six cases were as follows. (1) Anaemia, which may be the only symptom; it can be absent, and is seldom severe. It has been ascribed to replacement of the bone marrow, to an inhibitory 'toxic' effect of the abnormal cells, to both these factors, or to renal failure attributed to Bence-Jones proteinuria. (2) Excessive rouleau formation, which is more characteristic of multiple myeloma than is anaemia. This condition has also been called 'autohaemagglutination' and the smears as 'greasy'. (3) Immaturity of both erythrocytes and leucocytes. (4) Lymphocytosis. (5) Eosinophilia. (6) The presence of myeloma and atypical plasma cells. Illustrations are shown of myeloma cells and some myeloma cells of reticulo-endothelial origin. Plasma cells were regarded as atypical when they were related to the myeloma cells morphologically, but had lost their nucleoli. In nineteen of the fifty-six cases in which a diagnosis of multiple myeloma was made the diagnosis was confirmed by pathological examination. The authors conclude that the blood smear can be a valuable help in the diagnosis of multiple myeloma, that the plasma-cell type of multiple myeloma is truly predominant in frequency, and that multiple myeloma is probably closer to leukaemia than to neoplasia.

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 Mouissette, L., and Watkins, C. H. (1942) *Proc. Mayo Clin.*, **17**, 433.
 Putti, V. (1927) *Chir. Organi Mov.*, **11**, 335.

BRAIN ABSCESS

See also B.E.M.P., Vol. II, p. 597.

Clinical picture

Abscess in the sella turcica region

Simulating a primary tumour of the pituitary gland.—H. J. Svien and J. G. Love record the very rare occurrence of a primary abscess within the sella turcica, which simulated a primary tumour of the pituitary gland and was cured by operation. The patient, a woman aged thirty-four, had been for fifteen years the subject of nasal obstruction and polypi, and the condition was further complicated by diabetes insipidus and by severe left-sided headache which had been present for four years. Radiologically the sella turcica was enlarged and there was some erosion of its floor, and diagnoses of bitemporal hemianopsia and of a chiasmal lesion were made. A right transfrontal craniotomy exposed an abnormal mass which was anterior to the optic chiasmi and was between the optic nerves. To exclude the possibility of an aneurysm of one of the internal carotid arteries, a small spinal puncture needle was inserted into the mass and when it was withdrawn thin yellowish pus exuded. The capsule of the abscess was opened widely and crystals of sulphanilamide were introduced into the abscess cavity and around the optic nerves and chiasma. Post-operative convalescence was complicated by a sudden attack of anaesthesia and paralysis of the left side of the body; this condition disappeared spontaneously after a few days and was ascribed to vascular spasm of the right side of the circle of Willis. The authors do not exclude the possibility that such a reaction may have been due to sulphanilamide although they have not previously noted it; they mention that it is the first time, and they think for the last time also, that they inserted sulphanilamide intracranially.

Treatment

Surgical

Description of technique.—R. V. López discusses the treatment of abscesses of the brain. This is essentially a surgical matter since if left to itself the abscess will lead to death as the result either of increased intracranial pressure or of generalized meningo-encephalitis. Abscesses situated in the temporal or occipital lobe have a particularly serious effect upon the intracranial pressure because they may produce obstruction of one of the ventricles or of the Sylvian aqueduct, with consequent hydrocephalus. The most common cause of brain abscess is otitis media or mastoiditis, which is present in 83·2 per cent of cases. Affections of the nose or accessory sinuses account for 9·1 per cent, and the remaining 7·7 per cent arise as a complication of cranial injury or metastatically from some remote inflammatory lesion. In the early stages the abscess does not have a capsule; it is surrounded by an area of acute encephalitis and this again by a zone of oedema. Various operative procedures have been advised and the choice must depend upon the conditions present in each individual case. Simple puncture through a small trephine hole after the dura has been sutured to the skin is recommended by Dandy, who points out that what kills the patient is increased pressure. The author has had favourable results from this treatment, which is very simple and is associated with a minimum of operative trauma. Closed drainage by introduction of a catheter through a small trephine hole may be substituted but this procedure is attended by a risk of leakage round the tube and by the danger of meningitis. Open drainage is suited to chronic encapsulated abscesses but may be followed by herniation of the brain, a serious and frequently fatal complication. Of a series of thirty-six patients, treated by the author ten died. Some authorities advocate an operation in two stages. At the first operation craniectomy is performed and this is followed by herniation of the brain through the opening and the formation of adhesions shutting off the subdural space. At the second operation the abscess is opened. The author advises the two-stage procedure only in cases of abscess secondary to osteomyelitis of the cranial bones. The necrotic bone is removed at the first operation and diathermy applied to the dura to ensure the formation of adhesions. Total extirpation is advisable when a firm capsule is surrounded by a zone of encephalitic softening enabling it to be shelled out easily. Rapid healing follows.

López, R. V. (1943) *Schweiz. med. Wschr.*, **73**, 380.

Svien, H. J., and Love, J. G. (1942) *Proc. Mayo Clin.*, **17**, 497.

BRAIN: REGIONAL DIAGNOSIS

See also B.E.M.P., Vol. II, p. 609; and Cumulative Supplement, Key No. 188.

Symptom-complexes associated with:*Supratentorial lesions*

Diagnosis by olfactory tests.—C. A. Elsberg and H. Spotnitz have analysed the results of olfactory tests in 1,000 patients, the tests having been devised by Elsberg for the localization of supratentorial disease. The average normal figures were determined by large numbers of experiments on normal subjects. Pressure on the external olfactory pathways causes elevation of the value for the minimal identifiable odour; interference with the internal olfactory pathways prolongs the refractory period (that is the period after testing before which the subject can again identify the odour) on the same side as the lesion. The patient's full cooperation is essential, and in 126 of the 1,000 cases cooperation was poor or questionable. In 341 subjects (34.1 per cent) the values obtained were within normal limits; in 257 of these patients, signs of an intracranial lesion were either lacking or pointed to diffuse or to supratentorial disease, but in eighty-four patients localized supratentorial lesions were present although the olfactory tests were negative. The eighty-four patients included nineteen with a pituitary gland tumour confined beneath the sellar diaphragm and sixty-five in whom some part of the cerebral hemisphere or of the extracerebral olfactory pathways must have been involved. Seventy-seven patients had complete anosmia; thirty-two gave a history of trauma. Twenty-three patients with anosmia had a supratentorial tumour, and in 91 per cent it was frontal, temporo-frontal or temporal. Unilateral or bilateral elevation of the value for the minimal identifiable odour occurred in 239 patients, in 111 the cerebral lesion was diffuse or could not be localized clinically; of the remaining 128, the test correctly localized the lesion to the frontal or adjoining part of the temporal lobe in 71 per cent. Tests for prolonged fatigue alone gave correct results in 54 per cent. Complete olfactory tests were carried out in 251 patients with verified localized lesions; localization was correct in 41 per cent, incorrect in 5 per cent and in 42 per cent olfactory evidence of a localized lesion was not found. Elsberg's tests are therefore of limited value for the localization of supratentorial lesions; they are admittedly valueless in subtentorial disease.

Elsberg, C. A., and Spotnitz, H. (1942) *Arch Neurol Psychiat, Chicago*, **48**, 1.

BRAIN TUMOUR

See also B.E.M.P., Vol. II, p. 619; and Cumulative Supplement, Key No. 189.

Clinical picture*Localized headache*

Tumours of the Gasserian ganglion.—J. G. Love and H. W. Woltman report two cases of unsuspected tumour of the Gasserian ganglion which were encountered during operation for trigeminal neuralgia. One other case was seen at the Mayo Clinic in 1930, in a woman aged forty-nine. All the three cases had in common one atypical symptom, the presence of aching pain in the face, in the interval between the acute paroxysms. Gasserian ganglion tumours usually give some objective indication of their presence, such as sensory impairment or motor weakness. Of the authors' patients, both were women, aged respectively fifty-nine and sixty-six. Neither showed any neurological abnormality. In the first patient, a small epidermoid tumour lay within the posterior sensory root; the tumour was removed and the lower sensory fibres, which were injected and matted together, were divided. In the second patient a meningioma occupied most of the posterior root of the ganglion which, including the motor fibres, was resected with the growth. In both cases relief was immediate and complete.

Special methods of examination*Ventriculography and encephalography*

Successful operation.—R. A. Money reports the following case. A man aged forty complained of a lump on the forehead, first noticed at the age of five. It had grown steadily larger and he had lately suffered from headaches and a feeling of pressure inside his head. He was found to have a large bony tumour of the frontal region which was shown by X-rays to be causing deformity inwards as well as outwards. Encephalography showed some deformation of the anterior horns of both ventricles. No evidence of increased intracranial pressure was obtained and the cerebrospinal fluid was normal. Operation was carried out in three stages. The external tumour was found to be fused on the inner surface with a solid tumour in the region of the longitudinal sinus. The mass was removed. The longitudinal sinus did not require ligation. Histologically the bony tumour was found to be an osteoma, the intracranial tumour a meningioma. Bone grafting was not considered necessary. The patient made a good recovery with some subsequent regeneration of bone. He was well two and a half years afterwards, and encephalography did not show any deformity of the ventricular system, nor was there evidence of increased intracranial pressure. The cerebrospinal fluid was normal.

Differential diagnosis*From other conditions*

Main features of cerebral tumour.—G. Horrax reviews the present position of the diagnosis and prognosis of cerebral tumours. As regards diagnosis two questions must always be borne

in mind. (1) Has the patient a brain tumour or some other form of intracranial lesion which imitates a tumour? With present neurological knowledge and diagnostic methods this can be settled in practically every case, provided the patient or his responsible relatives consent to thorough diagnostic measures. (2) If a tumour is present, what is its site and what is its pathology? Here again the site of the tumour can usually be settled; but its pathological nature, which can be predicted in a large and ever increasing percentage of cases, often cannot be determined before operation. From the point of view of diagnosis there are, generally speaking, two clinical types of cerebral tumour. (a) those with the classical symptoms and signs of cerebral tumour; and (b) those with many different neurological and other findings but lacking the usual text-book picture. Among cases in the latter category are those comprising the so-called syndrome of increased intracranial pressure without tumour syndrome, or pseudo-tumour or arachnoiditis; and malignant hypertension. A warning is thrown out against lumbar puncture as a diagnostic measure in probable brain tumour; it is rarely needed, and the danger is real. As regards localization and pathology cerebral tumours fall into the following classes. (1) Tumours often but not always benign, such as meningiomas, acoustic neuromas, cholesteatomas, slow-growing gliomas, pituitary adenomas and pinealomas; these tumours are readily localized. (2) Tumours which seldom give any neurological evidence of their position. This group may include large infiltrating gliomas, and tumours in the region of the third ventricle; for their localization, air ventriculography may be needed. The prognosis for a permanently useful life in a patient harbouring a brain tumour depends on complete removal of the growth without damage to important neighbouring structures. Some tumours grow very slowly and partial removal may result in several years of freedom; but now, with improved modern equipment including electrosurgery and a well organized neurosurgical team, the position is much better, even regarding infiltrating tumours. Radiological treatment for patients with malignant brain tumours, with the exception of medulloblastomas, pinealomas and occasionally oligodendromas, has been completely disappointing. The figures of H. W. Cushing and L. Eisenhardt show that of 2,000 patients about 1,500 survived operation, and of these almost one-third had lived for from five to twenty-eight years. Among his own revised series of 400 verified cases Horrax found that, as would be expected, in the most favourable cases well over half were benign growths, namely meningiomas, acoustic neuromas, pituitary adenomas, gliomatous and haemangiomatic cysts of the cerebellum. In general terms Horrax therefore concludes that somewhat over one-half of all brain tumours are favourable for complete extirpation, and of those patients who survive operation about three-quarters should return to useful life.

Cushing, H. W. (1932) *Intracranial Tumours. Notes upon a series of 2,000 verified cases with surgical mortality percentages pertaining thereto*, Springfield, Ill.

Eisenhardt, L. (1937) *Tumors of the Nervous System*, Baltimore.

Horrax, G. (1943) *Bull. N.Y. Acad. Med.*, **19**, 125.

Love, J. G., and Wolman, H. W. (1942) *Proc. Mayo Clin.*, **17**, 490.

Money, R. A. (1943) *Med. J. Aust.*, **1**, 184.

BRAIN: VASCULAR DISORDERS

See also B.E.M.P., Vol. II, p. 641; and Cumulative Supplement, Key No. 190.

Cerebral atheroma

Arteriosclerotic Parkinsonism, arteriosclerotic muscular rigidity

Treatment.—H. Vollmer has studied the effect of various drugs in Parkinson's syndrome. A combination of 90.2 per cent hyoscyamine hydrobromide, 7.4 per cent atropine sulphate and 2.4 per cent scopolamine hydrobromide, known as compound "RT" and found to give good results in Parkinson's syndrome, was tested against the following solanaceous alkaloids. (1) Atropine, of nine patients who were treated by atropine for varying periods only two were slightly improved. After RT administration all improved, eight being markedly better. (2) Scopolamine: twenty-one patients were given scopolamine; slight or temporary improvement took place in four. All improved, twelve notably, on RT. (3) Hyoscyamine: fourteen patients treated by RT were then given hyoscyamine hydrobromide; all became worse. Of nineteen patients who had been treated by stramonium for a considerable period, with slight or temporary resultant improvement in only five, all were relieved, thirteen considerably, by RT. Various other combinations which were tested all proved inferior in efficacy to RT. Toxic symptoms were not observed after its use.

Vollmer, H. (1942) *Arch. Neurol. Psychiat.*, Chicago, **48**, 72.

BREAST DISEASES

See also B.E.M.P., Vol. II, p. 657; and Cumulative Supplement, Key Nos. 191–197.

Inflammations and their treatment

Acute mastitis and breast abscess

Aetiology and treatment.—Twenty-six cases of acute puerperal breast abscess are reviewed by A. I. S. Macpherson. Four patients were known to have had cracked nipples but, since three had attempted to wean the baby, it is uncertain how much importance should be

attached to this factor. Attempts to suppress lactation had been made by eleven patients; an interval of about two weeks usually occurred before trouble started. In ten further cases evidence was obtained that the breast had been only partially emptied at each feed. These two groups of cases indicate the aetiological importance of milk retention and stasis. Fifteen cases occurred within a month of parturition. In four cases both breasts were affected. *Staphylococcus aureus* was found in eighteen out of twenty cases investigated bacteriologically. In the majority of cases a source of sepsis could not be found, but the general condition was poor in all but one patient. Treatment consisted in incision and packing, the dressing being left undisturbed for at least five days, a procedure which, it is claimed, increases the patient's comfort, accelerates healing and reduces the chances of recurrence and of infection of the other breast. When the abscess was large or deep, lactation was cut short by oestrogen administration; otherwise it was allowed to continue.

Tumours and their treatment

Malignant tumours

Carcinoma.—C. D. Haagensen and A. P. Stout review the results of treatment in 640 cases of cancer of the breast in which radical mastectomy was performed. Of these patients twenty died as the result of the operation and 597 others were kept under observation until death or for a period of five years. Patients dead in under five years included 290 who died of recurrence, twelve who died of intercurrent disease without sign of recurrence and thirteen who died from unknown causes. Thirty-three were alive with recurrence and 231 were alive without recurrence five years after operation. This gives a five-year survival rate without recurrence for the 640 cases of 36.1 per cent. Preliminary biopsy does not appear to prejudice the results of operation. Local recurrence is very frequent, occurring in 22.8 per cent of the 640 patients within five years. The incidence might possibly be reduced by more extensive operations.

Carcinoma and X-ray therapy.—F. E. Adair compares the results of four different methods of treatment in operable cancer of the breast. (1) Surgery only was employed in 194 cases. When the axillary glands were not involved the five-year survival rate for the radical operation was 74.2 per cent. When axillary involvement was present the five-year survival rate was 47.3. A few patients were treated by simple mastectomy or even local excision of the tumour with surprisingly good results but the numbers are too small to be of statistical significance. (2) Pre-operative irradiation followed by radical mastectomy was used in 582 cases. Of 236 patients without axillary involvement 69 per cent survived for five years; of 337 with axillary involvement 35.3 per cent survived for five years. (3) Radical mastectomy and post-operative irradiation. For ninety-five patients without axillary involvement the five-year survival rate was 76.8 per cent; for 177 with axillary involvement the five-year survival rate was 41.8. (4) X-ray therapy alone was given to 182 patients. Only 24.2 per cent survived for five years. Comparing these four methods of treatment the best results appeared to be obtained by a combination of radical mastectomy with post-operative irradiation. The poorest results in this series followed irradiation alone.

An analysis of histories in inoperable cases.—W. C. MacCarty, Jun. and E. T. Leddy report ninety-eight cases of inoperable primary ulcerating carcinoma of the breast, treated at the Mayo Clinic by radiotherapy, during the fifteen years 1925–40. The reason for delay in seeking advice was in most cases stated to be absence of pain; the mere presence of a lump was not considered serious. Forty of the patients had not sought medical opinion before admission to the Clinic. The remaining fifty-eight had seen their doctors after an average delay of 15.5 months; twenty-five were given sound advice, the other thirty-three received treatment, including local applications, diet, electrotherapy and so forth, or advice which resulted merely in waste of time. Seventeen patients had consulted a doctor when they first discovered a lump; only five were advised to undergo an immediate operation—advice which was not observed—and twelve were ill advised or were unsuitably treated. As the authors point out, the need to educate doctors as well as the public appears to be urgent. The patients were generally treated by the 'converging beam' method, 130 kilovolts, 6 milliamperes, 40 centimetres target-skin distance and 6 millimetres aluminum filtration being used in the majority. At the end of the period of study forty-three patients had died and twenty-four had been lost sight of and were probably dead. Twenty-four had improved; in twenty-three the ulcer healed and in two cases the whole growth disappeared. Seven were made worse. The results of the study show that palliative radiotherapy is worth while.

Paget's disease of the nipple.—J. P. West and W. F. Nickel review the records of twenty cases of Paget's disease of the nipple. The cases fell into two groups, as originally described by J. Ewing. (1) Patients without any tumour of the breast detectable on clinical examination, but with an eczema of the nipple of long standing. (2) Patients complaining of a tumour of the breast and in whom the lesion of the nipple is relatively inconspicuous. The first group included thirteen patients, the average age being 57.5 years; in only three of these cases had the lesion of the nipple been present for less than a year. Section of the breast after removal showed a tumour in eight cases, and in three of these the axillary glands were invaded. The ten patients who were without axillary metastases at the time of operation, all but three of whom had been operated on more than three years before, and two more than fifteen years previously, were alive and well at the time of the survey; the prognosis in the above group is therefore

relatively good. The second group comprised seven patients, the average age was 47·1, and the longest history of a tumour was nine months; in five cases the axillary glands were involved. Four of the patients died within three years after radical operation, one has survived a year but has had a recurrence, and two cannot be traced. The prognosis in this group is poor. A close relation evidently exists between Paget's disease and cancer of the breast, and radical mastectomy should be practised in all cases whether or not a palpable tumour co-exists.

Adair, F. E. (1943) *J. Amer. med. Ass.*, **121**, 553.

Haagensen, C. D., and Stout, A. P. (1942) *Ann. Surg.*, **116**, 801.

MacCarty, W. C., Jun., and Leddy, E. T. (1942) *Radiology*, **39**, 711.

Macpherson, A. I. S. (1943) *Edinb. med. J.*, **50**, 25.

West, J. P., and Nickel, W. F. (1942) *Ann. Surg.*, **116**, 19.

BRONCHIECTASIS, BRONCHIOLECTASIS AND BRONCHIAL SPIROCHAETOSIS

See also B.E.M.P., Vol. II, p. 682; and Cumulative Supplement, Key Nos. 199–201.

Bronchiectasis

Clinical picture

Causes and treatment.—S. S. Misra records some observations on bronchiectasis. The disease is now thought to be a sequel to atelectasis, and the left base is the part of the lung most commonly affected. Five varieties—cylindrical, fusiform, beaded, saccular and mixed—are distinguished by their radiological appearances after injection of iodized oil. Bronchiectasis is common in young children. The history is of recurrent attacks of broncho-pneumonia, usually responding well to sulphonamides but with persistence of physical signs between attacks. Adults usually complain of chronic cough and sometimes give a history of pneumonia with delayed resolution. In some cases recurrent haemoptysis is the chief symptom. The differential diagnosis from tuberculosis by repeated sputum examinations is important, and skiagraphy will confirm the presence of bronchiectasis. In prophylaxis and treatment postural drainage is of great value, and should be begun early in all children who have recurrent attacks of broncho-pneumonia and in adults who show delayed resolution in pneumonia; even in fully developed cases postural treatment may give relief. It must be continued for sufficiently long periods in some cases for life. Lobectomy or pneumonectomy may be considered in selected cases.

Misra, S. S. (1942) *J. Indian med. Ass.*, **11**, 308.

BRONCHITIS AND BRONCHO-PNEUMONIA

See also B.E.M.P., Vol. II, p. 696; and Cumulative Supplement, Key Nos. 202–207.

Acute catarrhal bronchitis

Aetiology

Effects of tonsillectomy on upper respiratory infections.—A. D. Kaiser, consultant in paediatrics, Rochester, New York, discusses the effect of tonsillectomy on respiratory infections in infants and children especially in those in the age group of three to seven years. He closely observed the incidence of respiratory infections for ten years in 4,400 children, half of whom underwent tonsillectomy and the other half of whom were not treated surgically. Tonsillitis is common in young children; of the total 4,400 children, approximately 38 per cent were the subject of repeated attacks of tonsillitis (at least two febrile attacks a year) during the first seven years of life. He concluded that the tonsils are responsible for many upper respiratory infections and that in such cases tonsillectomy should be performed. In some cases adenoids cause frequent colds and should then be removed with combined tonsillectomy. Further, the incidence of laryngitis, bronchitis and pneumonia are not diminished by removal of the tonsils and adenoids.

Broncho-pneumonia

Primary broncho-pneumonia

Aetiology, complications and mortality.—Esther Hendry has investigated a one-year series (186 cases) of pneumonia in children, aged four days to twelve years; 66·4 per cent of the patients were under two years of age. Throat swabs and sometimes nasal swabs were taken when the children were admitted to hospital and at intervals during the illness and after discharge. The type of pneumococcus present was determined by intraperitoneal injections into mice and by using the resulting peritoneal exudate for typing with Lederle's immune serums. All the thirty-three recognized pneumococcal types, except 28, 32 and 33, were shown to be responsible for the disease in one or more cases; type 33 was not tested for because the appropriate serum was unobtainable. Type 19 was the organism which was most frequently seen, and type 6 came next. Type 19 was responsible for a rise of incidence of pneumonia in May and August. Bad housing conditions appeared to increase the liability to infection, probably owing to overcrowding. The mortality in the author's series was low; in children under two, the rate was 19 per cent, in children over two, 3 per cent. It was higher in pneumococcal cases than in pneumonia due to other organisms. Treatment by sulphapyridine probably accounted for the low rate. No one type seemed to be especially associated with the complications that were observed (otitis media, empyema, meningitis, peritonitis and arthritis),

except that three of the six empyema cases yielded the type 1 organism. Swabs taken subsequently showed that the organism rarely persisted after the acute illness had subsided. Five children only had positive swabs two months after recovery; in three the organism was type 19, in two type 6.

Treatment

Physiological therapy.—A. L. Barach describes the successful treatment of four cases of broncho-pneumonia of unknown aetiology, and one case of lobar pneumonia which failed to respond to sulphonamides, urging that in such cases 'physiological' therapy may just turn the scales in the patient's favour. The measures employed were as follows. (1) Maintenance of a positive pressure in the lungs in order to prevent exudation of serum and pulmonary oedema, and to overcome any obstruction in the small bronchi. (2) Inhalation of pure oxygen or a helium-oxygen mixture, either intermittently or continuously. (3) Inhalation of vaporized solutions of neo-synephrine and epinephrine (adrenaline), the former for its vaso-constrictor action on the mucous membranes, the latter to allay bronchial spasm. A specially designed hood or mask is used to maintain a positive pressure and for administration of the oxygen mixtures.

Primary atypical pneumonia

Aetiological consideration.—R. P. Becker, of London, Ontario, provides a commentary on the present views of the nature of atypical pneumonia which has suggested a clinical change from the old-fashioned type of lobar pneumonia with an acute onset, due in 90 to 95 per cent of the cases to acute pneumococcal infection. In fact it is becoming increasingly obvious that of recent years the classical lobar pneumonia constitutes but a small part of the total of cases with a fulminating onset, pathogenesis, course and prognosis. The atypical pneumonias occur in childhood and in young adults during the course of a mild upper respiratory infection. The connexion of the secondary infection of the lungs by micro-organisms of low virulence is not a new disease but is the result of more detailed investigation, especially radiological, of the common cold syndrome; during the last five years more than 80 per cent of all new patients with primary pneumonia seen in out-patient clinics have suffered from various degrees of acute or chronic broncho-pneumonia. The following names have been applied to these cases: (1) unresolved pneumonia, (2) delayed resolution, (3) silent pneumonia, (4) chronic pneumonia, (5) interstitial pneumonia, (6) virus pneumonia and (7) pneumonitis. Although a sound basis for the recognition of a virus pneumonia, often with atypical clinical features, has been established, and is admitted by Becker who, like J. F. Meakins, has written on the same subject in the same issue of *The Canadian Medical Association Journal*, he does not do so with any great enthusiasm. He indeed concludes that 'no studies reported up to date have established a clear-cut virus aetiology for this class of broncho-pneumonia'. He believes that until there is available satisfactory laboratory evidence to the contrary these pulmonary infections should be explained on the basis of partial bronchial obstruction with distal infection. This condition should be sought for by radiological examination in all cases of pneumonia.

Aetiology and classification. H. A. Reimann, Professor of Medicine at Jefferson Medical College, Philadelphia, who has previously published reports on cases of virus or, as he now prefers to call it, viral pneumonia—the non-committal 'primary atypical pneumonia' aetiology unknown' of the American Medical Service—discusses the aetiology and classification of this form of lung inflammation, of which the number of cases appears to be as many as, or even more than, that of the pneumococcal form. Some writers regard the condition as a new disease; others consider that old authors described the cases as a variant of the influenza of 1918, of influenzal pneumonia, broncho-pneumonia, migratory pneumonia, interstitial pneumonia or capillary bronchiolitis. The viruses of psittacosis, vaccinia, variola, measles, influenza, varicella, lymphocytic choriomeningitis and a psittacosis-like disease (ornithosis) are referred to. For the disease in cats the name 'alourosis' is suggested by the author, who divides the viral pneumonias into two general groups: (1) that comprising the sporadic, non-seasonal, slightly contagious systemic disease, with a relatively long incubation period of from ten to fourteen days; (2) that characterized by large epidemics of mild, highly contagious local disease of the respiratory tract, commonly called colds, grippe or 'influenza'. All observers agree that the sulphonamides have not any favourable influence on viral pneumonias. Convalescent serum from patients who have had the disease has been employed, but without evidence of benefit.

Clinical picture and X-ray findings.—In the first three years of this war there were in the military district of London, Ontario, ninety-six cases of acute exudative lung disease which would presumably have escaped notice had the patients not been examined radiologically and silent broncho-pneumonic lesions discovered. P. M. Andrus found that the majority of subjects of this silent, concealed or undiagnosed broncho-pneumonia had recently had a cold, influenza or other similar indisposition, but were not seriously ill, although the erythrocyte sedimentation rate was often raised and the leucocyte count, in the few cases in which it was taken, was always elevated (12,000 to 35,000). The temperature was usually not raised. Fifty-four per cent of the cases were right-sided, and in 76 per cent the affected part of the lung was entirely below the level of the lower border of the hilum or the third costal cartilage. Reference is made to the twenty-nine similar cases recorded by H. Ramsay and J. G. Scadding during two years in a tuberculosis dispensary service.

Analysis of cases.—Under the above heading J. F. Meakins deals analytically with approximately 150 cases, eventually diagnosed as of lobar pneumonia, broncho-pneumonia or pneumonitis, of which it is safe to say that the great majority, more than one hundred, were examples of primary atypical aetiology. These patients were admitted into the Royal Canadian Air Force Hospital, St. Thomas, Ontario, between 15th June and 15th November, 1942. The cases of primary atypical pneumonia are thoroughly analysed, thus 91 per cent came only insidiously; 81 were mild and only 10 per cent were toxic during the course of the illness. The most prominent cause of complaint was cough, usually dry and hacking, only 13 per cent of the patients showing sputum on admission; 30 per cent complained of pain, distress or constriction of the chest; two-thirds of these had retrosternal discomfort, but no patient had true pleuritic pain; 40 per cent had signs of a cold in the chest or head. In 98 per cent the temperature fell by lysis, and in 2 per cent by crisis; the leucocyte count was below 10,000 in 73 per cent and below 1,500 in 26 per cent; the average stay in hospital was eighteen days. The bodily temperature was normal in ten days or less in 89 per cent. The radiological appearances were a hazy type of infiltration spreading out in a fan-shaped manner from the hilar region.

Primary atypical pneumonia

Report of the American Commission.—In 1941 numerous cases of an atypical pneumonia occurred in an army establishment in the United States of America, and a commission was appointed to investigate the outbreak. This commission reports that it examined all cases of disease of the respiratory tract admitted to the station hospital between 9th December, 1941, and 24th March, 1942 (244 in all) and scrutinized the records of all such cases admitted during the preceding year. Among a total of 1,188 records 228 cases of atypical pneumonia were identified and among the 224 patients examined sixty-nine came under the same head. The diagnosis of atypical pneumonia was restricted to cases in which a lesion of the lung was demonstrated by X-rays and in which no clinical or pathological evidence of pneumococcal or other known form of pneumonia was obtained. In the sixty-nine cases studied the onset of the illness was gradual, the symptoms were mild or moderately severe and constitutional manifestations predominated. Physical signs in the lungs were very slight, in contrast to the comparatively extensive pulmonary infiltration revealed by X-rays. The course was from five to fourteen days and was uninfluenced by chemotherapy. Complications were very rare and the prognosis was excellent. Only one of the sixty-nine patients died. The distribution by lobes was similar to that of pneumococcal pneumonia. During the summer of 1941 the incidence of atypical pneumonia appeared to be related to that of other acute respiratory affections, and the symptomatology and course of many of these cases were indistinguishable from those of atypical pneumonia. Unrecognized cases may constitute the source of spread of the disease. The Commission emphasizes the importance of frequently repeated radiological examinations in all cases of anomalous acute respiratory disease. All attempts to isolate the aetiological agent were unsuccessful. In the fatal case necropsy findings were those of haemorrhagic interstitial broncho-pneumonia.

Virus strains.—Primary atypical pneumonia appears to be a clinical but not an aetiological entity, being related to different viruses in different cases. F. L. Horsfall, Jun., E. C. Curnen, G. S. Mirick, L. Thomas and J. E. Ziegler, Jun. claim to have discovered yet another virus capable of causing the disease. Specimens from patients were used to inoculate different animal species. No obvious case of infection resulted, but animals inoculated with some specimens or with material derived by serial passage from these, developed antibodies against the 'pneumonia virus of mice' (P.V.M.). Twelve strains of a virus were recovered from twenty patients, and immunological evidence was obtained that each possessed antigenic components also present in P.V.M. Of these strains two were derived from throat washings, eight from sputum and two from plasma. The virus was filterable through Berkefeld V candles, retained its activity when stored at -70°C for six months, withstood repeated freezing and thawing and was inactivated by heating at 56°C for thirty minutes. The production in rabbits of neutralizing bodies against P.V.M. was less abundant and less rapid when the virus from cases of atypical pneumonia was used for immunization than when P.V.M. was used. Convalescent serums did not contain demonstrable quantities of antibodies against P.V.M., psittacosis virus, the virus of lymphocytic choriomeningitis or influenza virus. The mongoose infective virus, which appeared to be related to cases of atypical pneumonia studied in 1939, was found on re-investigation to produce antibodies against P.V.M. and the suggestion is made that the virus obtained in the present series of cases is either identical with or closely related to mongoose infective virus.

Chronic bronchitis

Treatment

Management of aged persons.—T. H. Howell points out that the treatment of chronic bronchitis in the aged has altered surprisingly little during the last sixty years. At the Royal Hospital, Chelsea, experience of such cases and of war-time restrictions on prescribing have led to certain changes being made in the routine treatment. The number of in-patient cases at the Hospital since the outbreak of war has been 110 and of out-patient cases 400. When the weather is cold an increase takes place in the amount of bronchial secretion and the men have to cough to bring it up instead of spitting at intervals as is their usual habit. As winter comes on the coughs of the bronchitic pensioners become worse and they have to be admitted

to the infirmary for treatment. If admission is delayed some of the patients develop bronchial spasm or pyrexia or both. In such cases the outlook is bad, for after one or two attacks congestive heart failure frequently supervenes, and responds poorly to treatment. Hence prevention of complications is of great importance. In cases in which broncho-pneumonia is even suspected sulphapyridine in adequate doses should be given. In old people pyrexia should be taken as the indication for specific therapy, and the development of clinically recognizable consolidation should not be awaited because irreparable damage to the heart may have occurred before signs appear in the lungs. The tendency to bronchial spasm is shown by the continued presence of rhonchi in the chest. The best treatment is adrenaline (epinephrine), $\frac{1}{2}$ to 1 cubic centimetre, by hypodermic injection; lobelia, belladonna and ephedrine by mouth are far less satisfactory. The effect of the injection usually lasts for from eight to twelve hours, after which it may be repeated. The duration of the acute attack is shortened by this method of treatment. Of a series of fifteen patients, all but one were free from spasm by the fifth day and all by the seventh day, whereas in previous winters each of them had been in the infirmary for periods varying from three weeks to three months. Careful watch was kept on the blood pressure and there was not any evidence obtained that it is raised by adrenaline. The blood pressure of an elderly chronic bronchitic tends in fact to be below the normal for his age and to fall still lower, regardless of adrenaline treatment, during the acute attack. Posture is of great importance. If the patient is constantly slipping down in bed and therefore cannot expand his lower chest properly the custom at the Royal Hospital is to nurse him sitting upright in a tall armchair. Every patient, as well as every doctor, has his favourite cough mixture. Patients mainly favour those containing compound tincture of camphor (tinctura opii camphorata [B.P.]) or chlorodyne (tinctura chloroformi et morphinae [B.P.C.]). A good plan is to give expectorants by day and opiates at night. But according to S. Alstead's work little is to be gained from expectorants and, in confirmation of this, Howell states that the most effective measure for producing sputum has been found to be the drinking of a glass of hot water before breakfast.

Review of therapeutics—Recent methods of treatment of chronic bronchitis have not produced any striking results. As F. H. Young observes, the treatment of the disease is very unsatisfactory owing to the conditions with which it is always associated, namely degeneration of the bronchial epithelium and emphysema. Many patients keep fairly well apart from the recurrent febrile attacks which occur in the winter. Vaccines, autogenous and stock, have been used for years in prophylaxis and in treatment but the effects of these, although occasionally dramatic, are more often disappointing. Sulphonamides also have given variable results. This may be due to the fact that the relapse is usually well established before the patient calls in his doctor and sulphonamide treatment is begun. Results may be improved by supplying some three doses of the drug to the patient in the interim period, with instructions to begin treatment as soon as signs of a relapse appear. The doctor when he calls can then prescribe whatever further doses may be necessary. The use of expectorants has always been empirical. In children they are effective in so far as vomiting is induced. Recent investigations in adults have failed to show that any measurable effect is produced on the quantity or composition of the sputum by the usual doses of ammonium carbonate or chloride.

EDITORIAL COMMENTARY—The Bronchitic Patient

When first called in to see a bronchitic patient, the physician will find him febrile, flushed and complaining of a raw feeling under the sternum. His temperature may be as high as 101° F. Physical examination may show very little, or rhonchi may be present over one or both lungs. There may also be slight dullness confined to a localized area of the chest. Such signs, however, may be indicative of other conditions as well as of bronchitis. Abscess of the lung may have, as its only physical sign, a few rhonchi over a localized area of the chest. The patient will have a high temperature and will look very ill so that a diagnosis of acute bronchitis would not be justifiable without further investigation. A complete blood count should be made; the sputum, if any, must be examined for specific organisms and elastic tissue and an X-ray examination carried out as soon as possible. A spontaneous pneumothorax of the pressure type which has caused the mediastinum to move across to the opposite side, thus constricting the one remaining lung and giving rise to râles and rhonchi, is also sometimes mistaken for acute bronchitis. Sudden massive collapse of one lung will often produce the signs of acute bronchitis in the opposite lung. In both instances X-ray and thorough physical examinations will demonstrate at once that the diagnosis is not that of acute bronchitis. Acute heart failure may simulate acute bronchitis but in most cases the diagnosis will be apparent from the cyanosis and distress of the patient.

Having satisfied himself that none of the above conditions is present and that the case is a straightforward one, the practitioner can proceed with the treatment. The temperature of the room must be kept constant; 60° F. to 65° F. is the best. This must not be attained by sealing the room, for good warmed fresh air is essential. Inhalations of compound tincture of benzoin three times a day are excellent in the acute stage. After two days or so the acute phase will pass and, if sputum is present, an expectorant mixture can be given. The patient should be kept in bed for at least two days after the temperature returns to normal, and to prevent relapses after getting up, it should take him at least a week to return to his normal amount of activity. A good routine for that week would be as follows. Getting up for two

hours on the first day, four hours on the next day, six hours on the third day, eight hours on the fourth day, all day on the fifth day; on the sixth day a short walk should be taken, and a longer one on the seventh; work could be resumed on the eighth day.

Chronic bronchitis is a most difficult disease to classify since the doctor must not diagnose a patient as a chronic bronchitic unless a thorough investigation has not shown any other disease of the lungs. What are the most common diseases likely to simulate chronic bronchitis?

(1) *Pulmonary tuberculosis* of the chronic fibroid type can be diagnosed by testing the sputum regularly and not being satisfied with one negative result, and by having an X-ray film taken at the first opportunity. (2) *Bronchiectasis* is more easily diagnosed when the patient is in a hospital. Purulent sputum and a foul taste in the mouth on expectoration should cause the practitioner to suspect bronchiectasis; the patient should be removed to a special centre for further investigation. (3) *Carcinoma of the lung* is indicated by an area of dullness and by absent or weak breath-sounds over the area of collapsed lung. An X-ray film will verify the blockage of the bronchi. Early diagnosis is essential in such cases because modern thoracic surgery can often effect a cure. Often one of the first symptoms is a little blood-stained sputum which should be tested regularly and, if this is negative, an X-ray examination should be made at the earliest opportunity.

The chronic bronchitic should live in as dry an atmosphere as possible and not in low-lying areas near rivers. High altitudes are not good for patients over middle age. An expectorant mixture, such as sodium bicarbonate 10 grains, sodium chloride 3 grains, spirits of chloroform 5 minims, aniseed water to $\frac{1}{2}$ ounce, should be taken in warm water by the patient when he wakes up in the morning. This will help to rid the bronchi of discharges which may have collected overnight. Breathing exercises are of great value in some cases of chronic bronchitis, especially those complicated by emphysema. The exercises should be carried out under the supervision of a trained person, preferably at a chest centre.

To sum up, it cannot be too strongly insisted how important is a thorough physical examination and X-ray examination of the chest if there is any doubt of the cause of the underlying bronchitis. Acute or chronic bronchitis should never be diagnosed, or drugs prescribed, until all other diseases likely to simulate it have been excluded.—GROFFREY S. TODD.

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BURNS AND SCALDS

See also B.E.M.P., Vol II, p 719; and Cumulative Supplement, Key No. 209.

Treatment

First, second, and third degree burns

Sulphadiazine spray. The advantages and disadvantages of the Pickrell treatment of burns by the sulphadiazine-triethanolamine spray are discussed by G. J. Coloviras, Jun., W. T. West and J. C. Armour. In this solution a coagulant is combined with a drug of strong chemotherapeutic activity. It has been used in eight cases, in four of which it was combined with sulphadiazine given by mouth. An aqueous solution containing sulphadiazine 3 per cent and triethanolamine 8 per cent was used for spraying. The burned area was first thoroughly cleaned with soap and water, and the spray was applied every hour during the first twenty-four hours, every two hours during the second twenty-four hours and every three hours during the third twenty-four hours. The eschar which results from solidification of the triethanolamine is a thin supple translucent structure. As compared with cases in which treatment with saline compresses is used, the length of stay in hospital is about the same, but the sulphadiazine method was found to be much easier to manage. The type of eschar produced is far less liable to crack than that produced by other coagulants, and the patient may therefore be allowed out of bed sooner. The solution has a high degree of bactericidal action on organisms commonly infecting burns. Pain is rapidly relieved. The method can be used for burns of the face. The solution is of very low toxicity, but some danger of poisoning might exist with very widespread burns. The chief disadvantage of the method is the slowness with which the crust is formed. As with other coagulation methods, subsequent skin-grafting is impeded.

Infected burns

Use of penicillin and of propamidine.—A. M. Clark, L. Colebrook, T. Gibson, M. L. Thomson and A. Foster have used (1) penicillin and (2) propamidine in an attempt to eliminate haemolytic staphylococci and streptococci from infected burns. Sulphanilamide, although effective in many cases, is not always successful, and when it is applied to large surfaces the danger of poisoning from absorption is real. A substitute was therefore sought. (1) Penicillin was applied as a powder in the first few cases but was found to cause too much pain. A solution was tried and was found unsatisfactory. A cream containing about 120 units of penicillin per gramme made up with lanette wax SX and castor oil was then adopted as the routine application. This cream has been used only for burns known to be infected with haemolytic streptococci or staphylococci or with both. It was thickly applied four times at intervals of forty-eight hours. No toxic effects were seen. In 76 per cent of fifty-four burns infected with streptococci the organism disappeared within five days and did not reappear. In seven instances the bacterial strain concerned was sulphonamide-resistant. In five cases of multiple burns one area was left without penicillin treatment. In every case streptococci persisted in that area, whereas they vanished from the treated areas. In the remaining 24 per cent complete elimination of streptococci was delayed, but in all cases penicillin appeared to exert a beneficial influence. Staphylococci also disappeared from many of the wounds, and better results would probably have been obtained if necessity to husband supplies of penicillin had not dictated the use of a comparatively weak cream. (2) Propamidine was used in the form of a 0.1 per cent cream in Mumford base. Four or in some cases five applications were made at forty-eight hour intervals. Of thirty-four burns treated, twenty-one (62 per cent) became free from haemolytic streptococci within five days. In eight cases the organism persisted, responding afterwards to penicillin. No toxic effects were observed. Coliform bacilli, *Bacillus proteus* and *Pseudomonas proteanica* were apparently unaffected by either propamidine or penicillin. Healing of the burns was rapid in most of the cases treated by penicillin and in nearly as many of those treated with propamidine.

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CANCER

See also B.I.M.P., Vol. II, p 737, and Cumulative Supplement, Key No 212.

Pathology and aetiology*Pathology of infancy and childhood*

Incidence of cancer among children in America—M. Ritvo, J. D. Houghton and E. J. McDonald have investigated the incidence of malignant tumours of infancy and childhood. The records of the Boston City Hospital for the period of twenty-five years ending in 1939 show that seventy-two children were treated there during that period for malignant neoplasms. The distribution of the tumours was as follows. Intracranial, twenty-three, or 32 per cent of the whole group, kidney, thirteen; bone, eleven; soft tissues, six; skin and mucous membranes, five; eye and orbit, four; adrenal (neuroblastoma), two; gastro-intestinal tract, two; lung, mesenteric glands, retroperitoneal glands, parotid, thymus and jaw (plasmocytoma), one each. Among the larger groups, the intracranial tumours included nineteen gliomas, one cranio-pharyngioma and three unclassified, possibly metastatic, growths. The renal tumours were Wilms's tumour in twelve cases, embryonal carcinoma in the remaining case. The bony tumours included seven osteogenic sarcomas and four Ewing sarcomas. The soft tissue tumours included one synovial sarcoma, two fibro-sarcomas, one leiomyosarcoma, one haemangio-endothelioblastoma and one undifferentiated tumour. Tumours of the skin and mucous membranes were one amelanotic melanocarcinoma, one melanoblastoma, three carcinomas of mucous membranes and one basal-celled carcinoma. Only three examples of carcinoma of the adult type occurred in the entire series. The only congenital tumour was a malignant teratoma of the orbit. Among the earliest instances of the occurrence of malignant disease were Wilms's tumour at the age of one year, medulloblastomas at one year and two years, and fibrosarcoma at two years. The number of children under fifteen dying of cancer in the United States of America during 1939 was 1,103, representing 0.7 per cent of the total deaths from cancer. In the Commonwealth of Massachusetts the death rate for cancer in childhood had risen progressively and in 1939 was greater than that for any other disease except 'influenza', diseases of the nervous system, appendicitis, diarrhoea and pneumonia.

Carcinogenic properties of sex hormones

Experiments on mice.—The Caldwell Lecturer for 1942, C. P. Rhoads, reviews the clinical and experimental data bearing upon the part played by sex hormones in the production of cancer. It has been shown that female mice of a strain with a high incidence of cancer of the breast transmit to their offspring in the milk a carcinogenic principle. If the young of such a mouse are suckled by an animal of a low cancer strain the incidence of cancer among them remains low. On the other hand, if new-born mice from a low cancer strain are suckled by an animal from a high cancer strain the incidence of cancer among them can be raised, as in one set of experiments, from 0 to 15 per cent. It was next shown that oophorectomy early in life in the mice of a high cancer strain regularly prevented the development of breast cancer. Other cancers were not prevented. The experiment was then tried of transplanting ovarian

tissue into castrated male mice of a high cancer strain and breast cancer developed in many of them. The discovery of the relation between the ovary and the anterior lobe of the pituitary body led to the next step—transplantation of anterior lobe pituitary material into female mice of a high cancer strain. As a consequence, cancer occurred earlier and more frequently than in control animals, but only if the ovary were present. The converse procedure, removal of the pituitary body in animals of a high cancer strain, failed to reduce the incidence of breast cancer, although atrophy of the breast occurred. This was an effect difficult to understand except on the assumption that by the time the animal has reached a suitable size for operation the changes ending in cancer have already occurred. The isolation of the oestrogens was followed by experiments showing that they were effective in producing breast cancer in male mice of high cancer strains. The experiment was tried of giving testosterone to female mice of a similar strain and it has been found that if it is given early in life breast cancer is prevented, but that in later life testosterone has no effect. Some evidence suggests that oophorectomy or irradiation of the ovaries in women may inhibit growth of mammary cancer. Beneficial effects have also been reported from male hormone administration. Recent experiments have shown that in the male, castration may greatly benefit patients with metastases from prostatic carcinoma, whereas administration of testosterone propionate makes them worse.

General review of the aetiology

The main carcinogenic factors.—Lecturing to the St. Louis Medical Society, J. B. Murphy discussed some of the more important facts which have emerged from recent experimental work on cancer. The first experimental approach to the cancer problem consisted in attempts at transplantation of tumours, and the chief facts that came to light were that the individual character and malignant property of the cells are maintained through years of transplantation into hundreds of successive hosts. Intimate contact between the host's tissues and the tumour does not lead to a cancerous transformation of the host's cells; that is in mammals no evidence has been found of an infective agent capable of inducing malignant changes in cells. Successful transplantation depends chiefly upon the absence of genetic differences between the tumour cells and the host's cells. Some tumours show such a high degree of specificity that they can be maintained only in animals of a particular strain. Specificity may, however, undergo sudden changes, probably due to a mutation, and it is tempting to think that the original change from a normal to a malignant cell may represent a similar mutation. The part played by genetic factors in the causation of cancer varies in importance in different types of growth. Investigation of cancer strains in animals has shown that the inherited tendency to develop cancer is not a characteristic of the animal's cells in general but is confined to some one particular organ or tissue. Some evidence has been obtained that a similar disposition can be found in man. Thus when cancer occurs in one of a pair of identical twins a similar growth occurs in the other in over 50 per cent of cases. The hereditary factor can be modified by other factors, for example, the tendency to cancer of the breast in mice is found to be transmitted to a greater degree by the female than by the male and it has been shown that the intensifying influence is contained in the milk. Probably in all cases some additional factor is required to determine the onset of cancer in an individual disposed to it. The experimental induction of tumours by chemical agents known as carcinogenic substances has occupied the attention of many workers. Coal-tar derivatives have been shown to include numerous carcinogenic hydrocarbons. One, methylcholanthrene, is of particular interest because it is related to bile-salts, sex hormones and vitamin D. Lesions produced by X-rays, radium, ultra-violet light and certain infective agents and larger animal parasites have a tendency to become malignant. The mode of action of these carcinogenic agents is still unknown. The production by a dye (butter yellow) of liver cancer in animals only when the diet is deficient may furnish a clue in at least one instance.

Summary of causal factors

Chemical irritants and cancer.—A Honyman Gillespie lecture by F. E. Reynolds directs attention to various aspects of cancer. Considering how common the disease is, knowledge of it has increased remarkably slowly. Even now there has not been any definition suggested which will satisfactorily include all neoplasms. Two phases in the malignant process are recognizable, the phase of initiation and the phase of continuance. The author cites a case of rhabdomyoma. When first examined, the microscopical structure of the growth showed obvious resemblance to striped muscle fibres. The patient lived for six months and during that time portions of the growth removed for palliative reasons showed steady diminution of structural differentiation until shortly before death only spindle cells were observed. The cells of most sarcomas are round or spindle-shaped when the tumour is first seen and it is then impossible to guess what tissue the growth represents. Most of the work on cancer of recent years has been concerned mainly with causation. For many years the increased liability to cancer in certain industries has been recognized. The chemical irritants concerned are hydrocarbons belonging to three main groups: those related to dibenzanthracene; those unrelated to dibenzanthracene and containing the phenanthrene ring; and those not containing the phenanthrene ring. Emanations of radium are also known to be a factor in producing malignant growths. Recent work has shown that oestrogenic hormones are related to the development of mammary cancer in patients having an hereditary predisposition to carcinoma. Concerning human cancer the infective hypothesis has not received the support of the majority of workers. Viruses are known to cause malignant tumours in fowls

and have been claimed as the cause of certain tumours in mammals, for example the subcutaneous fibroma described by Shope in the cotton-tail rabbit. Hereditary disposition is now accepted as an aetiological factor in cancer.

Diagnosis

Dangers of delay in diagnosis

Responsibility of the family doctor.—C. R. Harms, J. A. Plaut and A. W. Oughterson point out that delay in the treatment of cancer is one of the chief reasons for the appalling death rate from this disease. The factors responsible for this delay were studied in a series of 158 patients. Of the total number only three presented themselves for treatment within a month of the onset of symptoms and these patients came rather on account of complications than because of cancer—one for intestinal obstruction and two for bleeding. The delay was two months or longer in 92 per cent of cases, and three months or longer in 84 per cent. The average interval between the onset of symptoms and the beginning of proper treatment was 8.46 months. The responsibility for this loss of time rested in 54.8 per cent of cases with the patient, in 17.4 per cent with the family doctor, and in 27.8 per cent with both. The chief reason why patients failed to seek advice was ignorance of the serious significance of the symptoms. The average delay for patients who thought they had breast cancer was half that for all cases of true breast cancer. This suggests that the delay might be halved if patients knew more about cancer.

Treatment

Fever therapy and irradiation

Routine of treatment and results.—Fever therapy combined with irradiation has been advocated in malignant disease as having greater destructive effect than irradiation alone. The method has been tested by H. S. Shoulders, E. L. Turner, L. D. Scott and W. H. Grant in a series of forty-two patients with inoperable tumours, all but nine of the latter verified by biopsy. The routine adopted was as follows. Preparatory treatment was given in the form of increased intake of fluid and chlorides; next came fever therapy and lastly X-ray therapy was applied. Fever therapy was given in a cabinet with the patient on an air-water rubber mattress placed over the heating element. The humidity of the cabinet was controlled by a small vaporizer. The patient's temperature was taken by a thermocouple inserted into the rectum and connected with an electrical recording thermometer. The temperature was raised to 104°–106° F. and maintained there for from thirty to sixty minutes. The patient, well wrapped up, was then taken to the X-ray room and given irradiation treatment. There were not any deaths as the result of treatment. Twenty-seven (65 per cent) of the patients showed symptomatic improvement. In some cases partial or complete disappearance of the primary growth or of metastatic lesions has been observed. One cancerous ulcer of the breast healed. The authors consider that their best results were obtained in the treatment of sarcomas.

Post-operative radiotherapy

Results in a series of 1,879 cases—R. McWhirter deals in a Honyman Gillespie lecture with the value of post-operative radiotherapy in cancer of the breast. The difficulty of comparing results in groups of patients treated by different methods is pointed out, together with the importance of including all, even the untreated, cases in any total from which percentage success is calculated. The author's figures relate to a series of 1,879 patients treated during the period 1930 to 1942. These cases included stage I, 556 (30 per cent); stage II, 325 (17 per cent); stage III, 374 (20 per cent); stage IV, 400 (21 per cent); stage not recorded, eighteen (1 per cent); recurrent carcinoma, not previously treated at the centre, 206 (11 per cent). Paget's disease without palpable glands was classified as stage I. The patients were divided into two groups according to the treatment given, whether radical operation alone or operation, radical or less extensive, followed by a full course of radiotherapy, that is the administration of not less than 3,500 r in three weeks. The basis of comparison was fixed as a symptom-free period of three years, since it was found that if a patient remained free from recurrence for three years she was likely to survive five years. The comparative numbers of patients conforming to this standard were as follows: stage I, surgery alone 54 per cent, surgery plus radiotherapy 76 per cent; stage II, surgery alone 28 per cent, surgery plus radiotherapy 60 per cent; stage III, surgery alone 21 per cent, surgery plus radiotherapy 44 per cent; stage IV patients were not compared because it was found that nearly all died within a few years whatever treatment they received. Thus post-operative radiotherapy can considerably improve the results of radical surgery. Simple mastectomy plus radiotherapy appears to give equally good results but further trials are necessary.

EDITORIAL COMMENTARY—Review of the Present-day Situation

The history of cancer research can be written in two chapters. Up to the outbreak of the war of 1914–18 clinicians and laboratory workers were interested in the nature of cancer; since 1918, the study of the induction of cancer artificially by means of chemical substances such as 3:4 benzpyrene, or by the application of physical agents such as X-rays or ultra-violet light, and the investigation of the nature and action of viruses have absorbed in ever increasing degree the energies of investigators. So great has been the effort to discover carcinogenic substances and to understand their modes of action, and so vast has been the increase in our knowledge of this aspect of cancer research, that it can be fairly said that the fundamental discoveries concerning the nature of cancer made by morbid anatomists and experimental

pathologists before 1914 are in danger of being overlooked and temporarily forgotten, to the great disadvantage of a rational outlook on therapy.

The labours of several generations of morbid anatomists and experimental pathologists are compressed in the statements that cancer is a disease of cells and not a disease of the body as a whole, and that the unlimited autonomous character of malignant growth is dependent upon the fact that the stimulus to multiply is inherent in the cancer cell itself. It follows from this that complete extirpation of the malignant cells results in cure of the disease. This conception of the nature of cancerous growths forms the justification for surgical treatment of cancer and no knowledge which has been gained in the last twenty-five years of intense investigation of cancer has in any way upset or altered the conclusions reached by pathologists prior to the outbreak of the war of 1914-18.

It might be thought, at first glance, that the discovery of filtrable tumours in which the causative action of viruses can be demonstrated must have altered fundamentally our basic conception of the pathology of cancer. This is not so. It was shown in the classical researches of Peyton Rous on the filtrable sarcomas of the domestic hen that after a sarcoma had been induced by injection of a small volume of cell-free filtrate, the clinical phenomena correspond exactly with those observed in cancerous disease generally. The virus particles which are injected induce sarcomatous transformation of the connective tissue cells with which contact is made, and then they apparently vanish and do not have any influence on subsequent events, which from this point onwards are completely explicable as a consequence of uncontrolled autonomous growth of the connective cells which have become infected. If the injection of filtrate is made intradermally the resulting tumour forms in the skin and can be observed as a small translucent mass within four days. When such a localized tumour is completely excised before the malignant cells have had time to extend to the underlying muscle, the animal is cured absolutely and lives for its natural term of life; when the operation is delayed it is not possible to remove all the tumour cells, and in such circumstances removal of the local tumour barely delays death from remote metastases. Thus it can be said with confidence that even in the exceptionally malignant tumours in which a virus aetiology has been established, the disease is confined to the infected cells and that complete surgical removal of the tumour leads to a permanent cure of the disease.

Widespread and inaccessible metastases cannot be dealt with by surgical methods and therefore the need for other methods of treatment presses urgently and incessantly on both clinician and laboratory worker. The conditions which must be met by any successful treatment are, from the nature of the disease, clearly of such a type that the remedy must have a selective lethal action on the cancer cells, normal cells being relatively unaffected. This limiting condition is not always borne in mind by investigators, as mentioned below. Although it is a commonplace in the history of therapeutics that empirical procedures have sometimes been attended with remarkable success—an example being the use of radium and X-rays in the treatment of cancer—it is usually advisable to bear in mind the pathology of a disease when considering suggestions for new methods of treatment. This applies particularly to cancer, of which the fundamental pathology is so exactly known. Examples of disregard of the pathology of cancer in experimental therapeutics are very numerous, but one line of research only needs to be considered and that because the underlying ideas appear to be accepted generally in default of criticism. The general line of research is briefly as follows. It is assumed that cancerous growth is merely excessive physiological growth; any differences which exist between the growth of a tumour and normal growth of the skin or bone marrow, for example, are quantitative and not qualitative. Growth of the body stops at a certain period of life and it is assumed, although never clearly stated, that this cessation of growth is brought about by the action of an internal secretion derived from the pituitary body, from the parathyroid glands, or from the adrenal glands. The proposition then is that this growth-controlling substance should be isolated and prepared in a concentrated form for administration in doses large enough to control malignant growth.

It should be observed in the first place that a confusion of thought appears to exist between the growth which leads to lengthening and general enlargement of the body and the multiplication of cells which continue throughout life and upon which the self-repairing mechanism of the body depends. In the second place if a growth-inhibitory substance could be found it would require to have inhibiting properties specifically effective against malignant cells in order to be useful in the treatment of cancer; otherwise, if growth in general were inhibited, bone marrow, skin, intestinal epithelium and other tissues indispensable for the continuation of life would cease to function.

To sum up, in spite of the great increase in our knowledge of cancer causation, no corresponding fundamental therapeutic advances have been made.—W. E. GYE.

Harms, C. R., Plaut, J. A., and Oughterson, A. W. (1943) *J. Amer. med. Ass.*, **121**, 335.

McWhirter, R. (1943) *Edinb. med. J.*, **50**, 193.

Murphy, J. B. (1942) *J. Amer. med. Ass.*, **120**, 107.

Reynolds, F. E. (1942) *Edinb. med. J.*, **49**, 663.

Rhoads, C. P. (1943) *Amer. J. Roentgenol.*, **49**, 289.

Ritvo, M., Houghton, J. D., and McDonald, E. J. (1942) *Radiology*, **39**, 278.

Shoulders, H. S., Turner, E. L., Scott, L. D., and Grant, W. H. (1942) *Radiology*, **39**, 184.

CATARACT

See also B.E.M.P., Vol. III, p. 1.

Acquired cataract*Symptomatic cataract*

The aetiology of diabetic cataract.—Since making examination of the lens a routine procedure in cases of diabetic coma, R. D. Lawrence, W. Oakley and I. C. Barne have observed that temporary opacification is a characteristic finding. This condition most commonly consists of a wavy gridiron pattern, as though the capsule were wrinkled in folds, but lines, streaks and larger opacities have also been noted. The evidence indicates that the appearances are due to alterations in the lens resulting from withdrawal of water. In a series of six patients with diabetic coma, four who showed signs of severe dehydration (sunken facies, haemoconcentration, systolic blood pressure below 80 millimetres Hg and ocular hypotension) also exhibited changes in the lens, and similar changes were observed in two non-diabetics with similar general symptoms of dehydration caused in one case by the vomiting resulting from intestinal obstruction, in the other by ulcerative colitis. The period of dehydration sufficient to produce lenticular changes has not been determined. The changes will disappear if the lack of fluid is made good by early saline administration, but tend to become irreversible as time goes on. The authors believe that dehydration of the lens is a factor in the production of permanent diabetic cataract of the acute juvenile type but that it is of doubtful importance in older patients.

Lawrence, R. D., Oakley, W., and Barne, I. C. (1942) *Lancet*, 2, 63.

CEREBELLAR DISEASES

See also B.E.M.P., Vol. III, p. 21.

Cerebellar atrophies*Atrophy of cerebellar cortex*

Report of a case.—Under the heading of 'cerebello-olivary degeneration, heredo-familial incidence', F. P. Weber, who reports the clinical features, and J. G. Greenfield, who describes the morbid changes found at the necropsy, bring forward the case of a woman aged seventy-eight. The disease began at the age of sixty with unsteadiness of gait. An interesting fact is that her mother died at the age of seventy-seven and evidently of the same disease; the age and mode of onset were also the same. The only children of the authors' patient who lived after childhood—two daughters, aged forty-five and forty-nine respectively—were found to be the subjects of a mild degree of the same disease which in both began at the age of forty with unsteadiness of gait. The authors' patient also suffered from weakness of the legs, some slurring of the speech, recurrent attacks of a kind of senile pruriginous purpuric eruption, almost limited to the left forearm and hand. When seen in 1941 she was in a state of progressive dementia, her sight and hearing had been failing, she was incontinent of urine and faeces and for the previous year had hardly been able to keep awake. It seemed clear that the heredo-familial nervous disease was a developmental abiotrophy, but it was possible that a diagnosis of a presenile encephalopathy might be present; the histological findings of Greenfield, however, settled the question in favour of parenchymatous cerebellar atrophy, together with extreme generalized arteriosclerotic changes. Among examples of familial developmental atrophy of the nervous system there are many family groups in which probably no histological examination has ever been made—for instance some of those in which tremor commencing after adult age slowly increases and ultimately tends to take on an 'intention' character, and in which the affected members live long and in some respects clinically resemble cases described as hereditary ataxia. The authors classify this case with those reported by G. Holmes and by A. J. Akelaitis. If the olivary degeneration is secondary to the degeneration in cerebellar cortex as the authors found to be so in their case, the term, cerebello-olivary, would be better than the term, olivo-cerebellar.

Akelaitis, A. J. (1938) *Amer. J. Psychiat.*, 94, 1115.

Holmes, G. (1907) *Brain*, 30, 466

Weber, F. P., and Greenfield, J. G. (1942) *Brain*, 65, 220.

CEREBROSPINAL FEVER

See also B.E.M.P., Vol. III, p. 39; and Cumulative Supplement, Key No. 223.

Prognosis*Mortality*

Results of chemotherapy.—G. E. Harries reviews five hundred cases of cerebrospinal fever treated at the City Isolation Hospital, Canton, Cardiff, from January, 1940 to 10th February, 1942 (two years and two months) by chemotherapy (sulphapyridine or sulphathiazole) without intrathecal injection of antineurococcocal serum. The total number of deaths was forty-three, or a gross mortality of 8.6 per cent. In cerebrospinal fever, especially in the acute fulminating form, death may occur within the first twenty-four hours, even within a few minutes of admission to hospital; if such cases are excluded the percentage mortality falls to 4.8. The ages of the patients ranged from six weeks (with complete recovery) to seventy years in a fatal case. In the age group, ten to thirty years, there were 179 cases with only four

deaths, or a case mortality rate of 2·2 per cent; in the subgroup of fifteen to twenty-five years of age, there were 104 patients with one death only, or less than 1 per cent. Among four patients over the age of sixty-five years there were not any recoveries. No one in attendance on the patients contracted cerebrospinal fever; masks were not worn, because the author believes that they dispose to nasopharyngeal congestion and to induce a temporary carrier state, with subsequent immunity. The administration of small prophylactic doses of sulphonamides in suspected cases had not any effect on the meningococci, except that the bacteria appeared to become drug-fast, and that large doses given later were then less effective. Sulphapyridine was given in 471 cases, and sulphathiazole in twenty-nine; the latter was found to be equally successful and less prone to cause nausea and vomiting. The following classification is proposed. (1) Meningococcal septicaemia: (a) acute fulminating with haemorrhages in the adrenal glands and other organs—for this form the author in 1940 proposed a new method of treatment; (b) chronic meningococcaemic. (2) Meningitic. (3) Encephalitic. In the whole series of 500 cases, 1,935 lumbar punctures, or an average of four each, were made. Of the strains of meningococci, 93 per cent were of group I.

Treatment

Chemotherapy

Sulphapyridine—A. Joe, in his Honyman Gillespie lecture, describes how advantage was taken of the Edinburgh epidemic of 1940–41 to make a trial of sulphapyridine in 500 cases of cerebrospinal fever. In all but a few cases the diagnosis was confirmed bacteriologically. An arbitrary scale of dosage was laid down, consisting of an initial intravenous injection of 2 grammes (30 grains) for patients over twelve years and of 1 gramme (15 grains) for those of from one to twelve years of age, and subsequently the oral administration of the drug in two-hourly doses for ten days, until a total of 49·50 grammes (742 grains) for patients over twelve and 24·75 grammes (372 grains) for patients of from one to twelve years had been given. To infants less than a year old the drug was given orally throughout the course, the total amount being 13·50 grammes (203 grains). If vomiting occurred the intramuscular route was adopted. The death rate in each age group was compared with the average mortality over a series of years prior to the introduction of the sulphonamides. The results were striking. The death rate among those less than one year old, for instance, was 27 per cent in the group treated by sulphapyridine and 87 per cent in the group not treated by sulphapyridine; in the group aged from ten to nineteen years, the figures were respectively 0 and 44 per cent, and in patients aged over fifty years, 58 per cent and 87 per cent; the general death rate at all ages was 18 per cent in the sulphapyridine group and 68·7 per cent in the non-sulphapyridine group. Two patients relapsed but both improved after a second full course of sulphapyridine. It was then decided to examine the cerebrospinal fluid before discharging patients from hospital, and a few with meningococci still present were discovered and were treated successfully by giving further sulphapyridine. Toxic phenomena included rash, drug fever, temporary anuria, albuminuria, haematuria, digestive disturbances and mental depression. In no case were the toxic disturbances sufficiently severe to interfere with treatment.

Use of sulphonamide drugs

Analysis of 3,000 cases.—Two papers, each dealing with the results of the modern (sulphonamide) treatment in more than three thousand cases of cerebrospinal fever in England and Wales appeared in the *British Medical Journal* on 24th April, 1943.

A. A. Jubb of the Ministry of Health analysed 3,206 cases, from 1913 to 1940. Between the peak years, 1915 and 1940, the smallest number was 301 in 1923, and the largest 2,157 in 1931. The prevalence remained at a low level from 1920 until 1929 when it began to rise, so continuing until 1931–2. After this there was a fall followed by a steady rise until 1939. In 1935 *prontosil* was introduced followed by *sulphanilamide*, and in 1938 I. F. H. Whitby found that *sulphapyridine* (M & B 693) was more effective than *sulphanilamide* against the pneumococcus, equally potent against the meningococcus and less toxic to the patient. This was a great advance, as *sulphapyridine* can be given promptly in a case of purulent meningitis while the bacteriological report about the meningococcal or pneumococcal origin is awaited. In March, 1940 in consequence of the good results received, the Ministry of Health issued a Memorandum (234/Med.) summarizing the most recent information. The fatality rate among 3,206 cases treated in hospital either by chemotherapy plus serum or by chemotherapy alone, and referring to those surviving more than twenty-four hours after admission, was 10·5 per cent; the rate in 849 patients treated by chemotherapy plus serum was 13·8 per cent. In the five years 1936–40 there was a steady decline in the fatality of cerebrospinal fever, the annual rates per cent being successively 63·8, 61·2, 50·6, 34·2 and 20·2; in 1941 the rate was 19·5, and in the first half of 1942 it was also 19·5. The disease is described as more deadly than deforming.

P. B. Beeson and Ethel Westerman analyse the data of 3,575 cases of cerebrospinal fever submitted to the Ministry of Health by more than a hundred hospitals in England and Wales covering the period of two years, June, 1939–June, 1941; a large proportion of the cases (2,738 or 76·6 per cent) occurred in the first half of 1940. The total number of cases notified in England and Wales during the same six months' period was 9,184. These figures supplement those reported above by Jubb. Among the 3,575 patients there were 570 deaths or 15·9 per cent; the ratio of males to females was 59·5 to 40·5 per cent; 45·5 per cent of the

patients were children under fifteen years of age. In the past the prognosis of cerebrospinal fever has been thought to be worse in infants and after the age of forty; the data available about sulphonamide treatment do not lessen, in fact they rather increase, the significance of age. The age group, fifteen to nineteen years, had the lowest death rate. The commonest complications were cranial nerve paralyses, arthritis and deafness; the cranial nerves most often involved were the third, fourth, sixth and seventh. Of the total 570 fatal cases, 217 patients, or 38 per cent, died within twenty hours of admission. Five different sulphonamide drugs were used: sulphapyridine, sulphanilamide, sulphathiazole, soluseptasine and pro-septasine. By far the most popular of these drugs was sulphapyridine, which was used alone in 86.6 per cent of the cases, and in combination with one of the other sulphonamides in an additional two hundred cases, or 95 per cent of the total. Sulphanilamide and sulphathiazole were the only other compounds used often enough to warrant comparison. The fatality rate for patients treated by sulphathiazole, alone or in combination, was the lowest—2.5 per cent for eighty cases treated in one hospital. With sulphanilamide, alone or in combination, there were eighteen deaths among 227 patients, a rate of 7.9 per cent. All but nineteen patients received sulphonamides, and 965 patients were given some form of specific serum treatment. The fatality rate for all patients was 15.9 per cent, for 2,591 patients who were given sulphonamides only, the mortality rate was 14.3 per cent; in an additional 965 cases, in which serum treatment was combined with chemotherapy, the mortality rate was 18.8 per cent; there was not any evidence that serum was beneficial.

Beeson, P. B. and Westernman, Ethel (1943) *Brit. med. J.*, **1**, 497.

Harries, G. E. (1940) *Lancet*, **1**, 522.

— (1942) *Brit. med. J.*, **2**, 423

Joe, A. (1942) *Edinb. med. J.*, **49**, 628

Jubb, A. A. (1943) *Brit. med. J.*, **1**, 501

Whitby, L. E. H. (1938) *Lancet*, **1**, 1210.

CHILBLAINS

See also B.E.M.P., Vol. III, p. 120; and Cumulative Supplement, Key No. 230.

Treatment

Employment of Bier's method

H. Hershheimer describes a series of twenty-four cases of chilblains treated by Bier's method of passive congestion. Most of the patients were schoolboys aged between fourteen and eighteen, the rest were adults. A Martin's rubber bandage 2½ to 3 inches wide was applied at the level of the middle of the humerus or femur just tightly enough to produce mild venous congestion. It was usually put on for the night, but in a few cases was worn for as long a period as twenty hours out of the twenty-four. Coldness and 'pins and needles' were avoided. Swelling of the hand was a sign that the bandage had been applied too tightly. Sixteen of the patients had suffered from chilblains in previous years in spite of various precautions. Of the twenty-four patients twenty-one were relieved completely in from five to seven days. Swelling and itching had disappeared, cracks had healed and the only remaining sign was redness of the skin. Treatment was nevertheless continued for at least six weeks, for when it was discontinued earlier, recurrence was found to take place. All these patients improved during a period of cold weather. In order to discount the possibility of spontaneous remission, none of the patients was counted as cured when improvement coincided with a spell of milder weather. To obtain further evidence of the effect of treatment, one hand only was treated in three patients suffering from chilblains of both hands, and in all cases the treated hand improved while the untreated hand grew worse. The reason why passive congestion is beneficial is difficult to understand; the suggestion is made that it acts by raising the pressure on the arterial side, which in its turn forces more blood through the capillary spaces of the limb and overcomes the tendency to stagnation which is found in chilblain subjects.

EDITORIAL COMMENTARY—Chilblains

In war-time, minor degrees of damage due to cold tend to sink into insignificance. In time of peace, frost-bite disappears and chilblains regain their importance as a common source of physical and mental discomfort. T. Lewis (1941) regards both ordinary chilblains and erythrocyanosis crurum puellarum as essentially similar to trench foot. In the absence of any histological knowledge of trench foot this cannot be regarded as certain, especially as Ungley and Blackwood have reported that persons subject to chilblains are not unduly susceptible to immersion foot. There is no doubt that in all this group the cause is damp chill rather than dry frost. Chilblains disappear with astonishing rapidity when damp cold weather gives place to a hard frost, to reappear as quickly when the temperature and humidity rise. It is this fact which has given passing credit to many useless methods of treatment. It is probable that the main predisposing cause of chilblains is undue spasticity of the skin vessels which, by failing to relax after the normal vasoconstriction of the extremities produced by cold, prolongs the anoxia to which the capillary walls are subjected, and thus increases their permeability.

The treatment of chilblains remains thoroughly unsatisfactory. There is no justification for the use of parathyroid tablets, for parathyroid extract is completely inactive by mouth. The

influence of calcium on capillary permeability has probably been exaggerated, and its use, whether orally or parenterally, is falling into deserved desuetude, its occasional apparent success being due to those remissions of symptoms which so often occur with changes in temperature and humidity. Much has been claimed for the injection of very large doses of vitamin D, the use of which rests upon a similar misunderstanding of the importance of added calcium to the health of the capillaries, but these claims lack substantial support. As one would expect, almost every endocrine gland has been accused of deficiency and gland extracts have been administered to excess, with more effect upon the patient's bank balance than on his or her toes. Ointments containing histamine and similar substances are advertised, but it is somewhat difficult to see how a substance which increases capillary permeability can be of any use in a condition characterized by excessive transudation. The same argument may be applied against the suggestion that Bier's passive hyperaemia may be effective. Nevertheless it must be allowed that this method has the advantage of simplicity and cheapness and therefore deserves trial.

At present physiotherapy appears to be the most satisfactory line of treatment. Many patients respond well to galvanic baths, even in damp weather. Those who do not must await the time when plentiful fuel will make prophylaxis possible. RAYMOND GREENF.

Herxheimer, H. (1942) *Lancet*, 2, 640.

Lewis, T. (1941) *Brit. med. J.*, 2, 837.

CHILD HEALTH AND WELFARE

See also B.E.M.P., Vol. III, p. 132.

Growth and development

Milestones of development

Outstanding changes.—H. Wissler describes the evolutionary period between birth and adolescence as consisting of alternating phases of activity and rest. The most striking of the active epochs is that which corresponds to puberty. Attention should not be focussed exclusively upon the sexual manifestations of puberty, important as these are. Other changes, both physical and mental, occur at this time. Growth is rapid, especially of the arms and legs, including the hands and feet. The face also shows disproportionately accelerated growth and its contours may change beyond recognition in a few months. Mental and psychological development also proceeds apace. All the changes should bear an orderly and harmonious relation to one another. The coordinating mechanism resides in the ductless glands, among which the sexual glands are of outstanding importance. They in their turn are dependent upon the anterior part of the pituitary gland; injection of the so-called gonadotropic hormone—which is identical in both sexes—leads, in immature animals, to the development of sexual characteristics. The thyroid gland also plays an important part. It is possible that some influence is exerted also by the adrenal and the pineal glands. A tumour of either of these glands is sometimes associated with precocious puberty. The brain stem is probably concerned also; precocity may accompany lesions of this region, for example, tumours of the floor of the third ventricle. Considering the complexity of the processes involved in puberty, disorders likely to need medical attention are rare. The liability to disease is not increased except for tuberculosis, which is apt to run a very malignant course. Minor disturbances include adiposity, which is an exaggeration of a normal process, and anorexia with wasting, which is seen almost exclusively in girls and is probably of psychogenic origin. Symptoms of circulatory instability such as palpitation and fainting sometimes occur. Psychological disturbances may lead to various forms of antisocial behaviour or hysteria, or may be due to an incipient psychosis (schizophrenia). Mind and body, moreover, are intimately related, and the doctor who is called upon to treat symptoms must realize that in many cases they represent a conflict between the adolescent and his environment.

Wissler, H. (1943) *Schweiz. med. Wschr.*, 73, 409.

COLDS

See also B.E.M.P., Vol. III, p. 271.

Aetiology

Smoking, dust and fog

Importance of paranasal sinusitis—The part played by mild or chronic paranasal sinusitis in producing the symptoms of the common cold has been studied by R. M. Dowdeswell. Of sixty patients suffering from the common cold, thirty-nine had only occasional colds or attacks dubbed 'influenzal'; in seven of these persons sinusitis had been diagnosed at one time or another. The remaining twenty-one patients had frequent or chronic colds, and sinusitis had been diagnosed in six of them. Only three of the patients in whom the diagnosis of sinusitis had been made had been operated upon for it. Symptoms suggestive of mild sinusitis were present in all the patients in the 'occasional cold' group. They included chronic postnasal catarrh; frontal, occipital or one-sided headache; sneezing attacks; nasal discharge, worse on one side and aggravated in certain positions; tenderness or slight swelling over one of the sinuses; pain in a sinus when the patient attempted to breathe in with the mouth or nose

closed; mild facial neuralgia. Cultures from the nasal discharge of patients with recurrent colds showed more or less normal flora when taken between attacks but yielded a heavy growth of some organism (*pneumococcus*, *Staphylococcus aureus*, *Streptococcus viridans* or Pfeiffer's bacillus) in pure or almost pure culture when taken during an attack. In two cases of recurrent colds the same organism was recovered in pure culture during separate attacks; in one case a pneumococcus type II was found, in the other Pfeiffer's bacillus. Sinusitis is probably much commoner in both children and adults than is generally recognized. The diagnosis of acute, severe cases is not difficult, but the mild, chronic or latent cases may present great difficulties in diagnosis. A negative X-ray is evidence only of the absence of empyema or of gross mucosal changes. The possibility of sinusitis should be considered in any case of febrile catarrh.

Treatment

Use of sodium sulphathiazole

Local and general application.—R. S. McArthur finds that very satisfactory results can be obtained in the common cold by local application of sodium sulphathiazole. The patients usually become free from symptoms within forty-eight hours, and many are completely relieved after the first night. The author uses a 3 per cent preparation in water-soluble jelly, which is packed in sealed collapsible tubes and applied by means of a special applicator so constructed as to deliver a measured dose of 7 minims of the jelly. This quantity is injected into each nostril three times a day, the last application being made at bedtime. If the treatment is not started until bronchial irritation has set in 1 cubic centimetre of the jelly given by mouth every few hours will relieve the cough. Pharyngitis can be relieved in the same way. If the nasal applications are started sufficiently early, laryngitis, pharyngitis and similar conditions are prevented from developing. The total dosage of sulphathiazole received during treatment by this method is quite small, each cubic centimetre of jelly contains about half a grain of the drug. The preparation is stable, because it is not exposed to light or air; there was not any apparent deterioration after eight months. Tests for toxicity were made upon rabbits, which were given daily colonic and nasal instillations in increasing doses. After six days the animals' blood pictures had not changed and nothing abnormal was found at necropsy. This method of treatment has been tried in over 200 cases of common cold. It was found that if the applications were begun at the onset of the cold relief was almost immediate. If the symptoms had become well established cure took two or three days. In all cases the patients were able to continue at their work, so that loss of time was avoided. The author emphasizes the importance of this from the point of view of war production.

EDITORIAL COMMENTARY—The Common Cold

Aetiology.—The common cold is the most frequent of human ailments; it has been estimated that in temperate climates 80 to 90 per cent of the population have at least one attack each year (W. H. Wynn, 1942) and the average has been placed rather higher, about two annually (E. W. Hurst, 1940). It is an autumnal and winter incident, and very few persons are naturally immune. In the last edition (1931) of the official *Nomenclature of Diseases*, drawn up by a Joint Committee appointed by the Royal College of Physicians of London, the common cold appears under 'Diseases due to Infection'. But the synonyms *acute rhinitis*, *acute coryza* and *acute catarrh* are more literally applicable to the old-fashioned streaming nasal discharge to distinguish it from other forms of sore throat such as tonsillitis and naso-pharyngitis. W. Osler and T. McCrae (1935) described it as *acute catarrhal fever*. Y. Kneeland, Jun. (1938) who worked with A. R. Dochez on the bacteriology of the common cold admitted that the defence of the common cold as a clinical entity was difficult; the clinical symptoms of allergic rhinitis often cannot be distinguished from those of a flare-up of a chronic sinusitis or of a common cold. There is obviously a close anatomical connexion between infection with inflammation of (a) the upper respiratory tract, and (b) the more restricted part of the nasal mucosa involved in the common cold. Inflammation may spread from the upper respiratory tract to the nasal mucosa, and both these areas may be involved together, or one after the other. For example, what begins in infants as catarrhal spasm of the larynx, or laryngitis stridulosa, may rapidly subside into a common cold, or the sequence of events may be reversed. In his account of 'silent' broncho-pneumonia, which can be diagnosed only by radiological examination of the lungs, P. M. Andrus (1942) found that the majority of the ninety-six young soldiers thus affected traced their illness to a previous 'cold, a bad cold, influenza, or sore throat'. This appears to have been an extension of infection from the upper to the lower respiratory tract. A common cold may precede a general disease, such as pneumonia, acute rheumatism, enteric or other exanthematous fever. Recurrent colds may be associated with local foci of infection, adenoids, chronic tonsillitis or dental sepsis. Disposing factors, such as excessive smoking, dusts, irritating gases, stuffy rooms, cold draughts and meteorological conditions, have been suggested. The importance of direct infection due to droplet-spread by sneezing or coughing is thoroughly recognized. The risk of reinfection or of chronic catarrh caused by the continued use of an infected ordinary handkerchief is an argument for the employment of a paper handkerchief which can be burned at once.

Bacteriology.—Much investigation has been carried out and a number of catarrhal bacteria at one time or another have been incriminated, some of which are among the normal flora of the throat. Opinion has now crystallized in favour of (a) a filtrable virus infection as the

primary cause of the common cold, and (b) secondary invaders—catarrhal bacteria—which do not cause the common cold but are activated by the virus and which are responsible for complications such as bronchitis, pneumonia and otitis media, and darken the prognosis. The bad effects of the common cold are due to complications, and not to the virus infection. In connexion with the subject of pneumonia as a complication of the common cold attention may be drawn here to atypical (virus) pneumonia or pneumonitis the varieties of which may be clinically indistinguishable yet may be caused by a number of known filtrable viruses. This subject has recently been reviewed by H. A. Reimann, W. P. Havens and A. H. Price (1942), the first of whom has followed cases of this kind since 1936.

In the Joseph Bancroft Memorial lecture on 7th June, 1940, before the Queensland Branch of the British Medical Association on 'Some Acute Virus Diseases of the Respiratory System', Hurst reviewed the bacteriological position of the common cold. Apart from human volunteers, the anthropoid apes provide the only available laboratory material for the study of the common cold; they are readily infected from human patients but are more prone to develop pneumonia. In 1914 W. Kruse concluded that a virus infection was the responsible cause of the common cold; this was confirmed by G. B. Foster, Jun. in 1916, and especially by A. R. Dochez, Katherine C. Mills and Y. Kneeland, Jun. in 1938. Experimentally, in chimpanzees, it has been shown that the incubation period after inoculation is about ten hours; symptoms then become worse for forty-eight hours, but recede until normality is reached after four or five days more. Clinically, however, and on other grounds, a longer incubation period, of thirty-six to forty-eight hours, has been found, this was the estimate in the arctic conditions of Spitsbergen where the average number of annual attacks is said to be one, or half of that in temperate climates (Hurst). In man and in the chimpanzee an attack of the common cold is followed by immunity for about three months. Wynn, from a survey of present knowledge about the common cold, divided the cases into two groups, the first consisting of primary colds due to a specific filtrable virus, distinct from that of influenza and also from that of herpes febrilis. The ordinary catarrhal organisms *Haemophilus influenzae*, pneumococci, haemolytic streptococci and *Neisseria pharyngis* are important as secondary invaders with activity and invasive powers which are increased by the virus and are mainly responsible for the complications such as bronchitis, otitis media and sinusitis. The second group included secondary colds, due to one or more of the secondary invaders, which are a legacy from repeated attacks of primary colds; the patients are carriers and the attacks are due to exacerbations of a persistent infection in local foci. The secondary colds are not so contagious or so prone to occur in epidemics as are the primary colds.

Prophylaxis. Exposure to infection by the virus should, as far as possible, be avoided by living an open-air life and using a mask when in contact with probable or possible carriers of the virus. Wynn advocates prophylactic measures from birth because many infants who among the poor suffer from colds when only a few weeks old, cannot easily localize infections and hence the bronchi are prone to be involved. If protected from colds during the early months of life, the infants acquire some immunity from frequent sub-morbid doses of infection. A nursing mother with a common cold should wear a celluloid mask, or cover her mouth and nose with a veil or folded handkerchief when near her infant. Vaccines made from patients with secondary conditions cannot logically be expected to benefit or protect against primary (virus) colds, but autogenous vaccines made from patients with secondary (bacterial) colds might lessen the liability to complications. Rooms have been disinfected by antiseptics, and sodium hypochlorite solution 0.5 or 1 per cent sprayed so as to form a bactericidal mist has been employed with success. The local application of the mixture, devised by W. Clegg (E. P. Poulton, 1932) for chronic nasal catarrh, of one part of soft paraffin and three parts of liquid paraffin, has been recommended for both the prevention and the treatment of the acute cold. The paraffin may act as a laxative, and a warning has been given that its prolonged use may cause lipid pneumonia (T. E. Walsh and R. P. Cannon, 1938). Wynn, who recently reviewed the treatment fully, did not find any material evidence of the power of quinine, aspirin, sulphapyridine and other drugs taken internally to abort acute colds; but refers to abortion of a primary cold by injection of a fairly large dose—200 millions—of an active stock vaccine.

Treatment.—Abortive and curative treatment of the common cold may, with benefit to all concerned including susceptibles, start with a day or two, or as long as there is fever, in bed. Those who have collected the 'cures' recommended, advertised or domestic, for the common cold, may be able to form a guess whether they, or those for other frequent symptoms such as constipation or cough, head the list; but a multiplicity of reputed remedies usually means that the really effective one has not been found.—HUMPHRY ROILESTON.

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COLITIS

See also B.E.M.P., Vol. III, p. 292.

Ulcerative colitis

Pathogenesis

Allergy.—A. H. Rowe suggests that allergy may play an important part in the aetiology of chronic ulcerative colitis, the latter representing, according to this concept, the most severe form of colonic allergic reaction. He reports seven cases in which complete and maintained relief took place when the patient was placed upon an 'elimination diet' omitting various foods. Three other patients obtained some relief, whereas another four did not show any improvement. In six of the control cases the subsequent test administration of certain foods caused diarrhoea. In one case pollen sensitivity appeared to be the causal factor. To investigate the influence of allergy in a case of chronic colitis it is advised that the patient be placed upon a cereal-free and fruit-free diet, in which tapioca, potato, lima bean or soya bean flour is substituted for other flours. Milk and beef are also omitted; soya bean milk may be used instead of ordinary milk. After from three to four weeks, if improvement occurs and is maintained, other foods are added gradually; a relapse is the signal for partial or complete exclusion of the food believed to be responsible. If relief does not take place after from three to four weeks, other elimination diets may be tried; the possibility of sensitivity to inhaled or to bacterial allergens should also be considered. In severe or intractable cases the study of a possible allergic cause should not be allowed to delay any surgical treatment which may be considered advisable.

Clinical picture

Aetiology, symptoms and treatment.—S. W. Patterson has studied a series of seventy-two patients with idiopathic ulcerative colitis, and records his conclusions. The cases fall into two groups, (1) the fulminant and progressive and (2) the prolonged relapsing type. The cause of the disease is unknown; psychogenic and allergic factors may play a part but the evidence that a diplostreptococcus is responsible is unconvincing. The onset is often insidious but it may be sudden. The most common symptom is diarrhoea, with the early appearance of mucus and more often of blood in the stools, the frequency increases until from ten to twenty motions may be passed in a day. Most patients have abdominal discomfort or pain and some have pain in the rectum. Gastric acidity is reduced. General symptoms of dehydration, malnutrition and toxic absorption develop. In the diagnosis amoebic and bacillary dysentery, mineral poisoning, organic disease of the colon and pulmonary tuberculosis must be excluded. The mortality varies from 10 to 40 per cent. The tendency to relapse is great. As regards treatment, rest is the most important factor. Severe cases should be treated in hospital. Rest in bed should continue until the stools are free of blood, until anaemia has disappeared and until the temperature remains normal. Nutrition must be improved by a diet consisting mainly of protein. National bread with its extra vitamin B content is recommended. Anaemia should be overcome by the administration of iron and, if necessary, by blood transfusions, and vitamin deficiencies should be made good. Colonic douching is sometimes beneficial. Drugs such as bismuth should be given and intestinal antiseptics may be tried. Sulphaguanidine and other sulphonamide derivatives are of great value in early non-toxic cases. Hydrochloric acid should be given to correct subacidity. Surgical treatment is needed when complications occur. In selected chronic cases permanent ileostomy offers relief and should not be delayed too long. Complete colectomy in two stages has been done in some cases. The operative mortality, however, is high.

Treatment

By colectomy.—H. Devine describes a case of very severe ulcerative colitis treated by colectomy. A woman aged forty had been ill for six months with diarrhoea and anaemia when an acute attack was misdiagnosed as appendicitis and led to an emergency appendicectomy. After the operation she grew rapidly worse, passing large quantities of blood, and became so emaciated and anaemic that repeated transfusions alone kept her alive. A barium enema disclosed a rigid colon, with no haustral markings, and a narrow rectum. Colectomy in stages was decided upon. At the first operation the ileum was divided four inches above the caecum. Both cut ends were brought to the exterior and the proximal segment was sutured to the side of the rectosigmoid junction. The sigmoid was divided, its lower cut end implanted side by side with the proximal cut end of the ileum, its upper cut end also brought to the surface. The excluded colon was washed out daily. After a month the ileo-rectal spur was crushed and a month later the cut proximal end of ileum and distal end of sigmoid were closed. Some months later, when the patient's general condition had enormously improved, the colon was removed. Some time later she was reported as being almost quite well.

Ileostomy.—R. Maingot advocates ileostomy in ulcerative colitis which proves refractory to medical treatment or when complications such as fistula, obstruction and so forth develop.

He uses the following technique. Through a vertical incision splitting the lower half of the right rectus muscle a portion of the ileum consisting of the last two feet is withdrawn and a point well above the site of the disease is chosen. The mesentery is divided cautiously on each side to mobilize the loop, the blood vessels being tied. Curved artery forceps are passed through a stab wound at the outer edge of the rectus muscle and are used to clamp the distal end, the proximal end being clamped through the first incision. The loop is divided by the cautery between the clamps. The distal end is drawn through the stab wound and is left clamped for five days. The cut mesentery of the proximal end is stitched to the peritoneum; the wound is closed, the clamp is removed from the bowel and a tube is inserted. The continuity of the bowel is restored later if cure ensues.

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COLON, CARCINOMA OF

See also B.E.M.P., Vol. III, p. 317.

Morbid anatomy

Association with adenomatous polyp

Familial polyposis—A family suffering from polyposis of the colon is described by V. S. Falk; it consisted of seven individuals, all but one of whom were affected. The father had died of carcinoma of the rectosigmoid region at the age of forty-eight, after suffering for twenty-four years from diarrhoea with passage of blood and mucus. The paternal grandfather was said to have died of 'cholera morbus' at thirty—a suggestive history. The eldest child, a male aged thirty, had a carcinoma of the descending colon which was successfully removed, and later a partial colectomy was performed but the man died from carcinoma of the rectum; X-ray examination showed multiple polypi of the rest of the large intestine. The second child, a male, died at twenty-eight from diffuse adenocarcinoma of the rectum after partial colectomy had been performed. The third, fourth, fifth and seventh children (one male, three females, ranging in age from twenty-six to ten) were found to have polyposis and were advised to undergo total colectomy. One consented, and the preliminary ileostomy has been done. None of the patients under twenty-three had any symptoms. In the sixth child, a male of eighteen, no evidence of polyposis was revealed by clinical, radiological or sigmoidoscopic examination. The author urges early and radical operation in such cases.

Treatment

Surgery

Carcinomatous sigmoido-vesical fistula—C. W. Mayo reports a case in a medical man, aged thirty-three, in order to show that the above condition is not always inoperable. The patient was admitted to hospital in July, 1941 with a history of having had in December, 1940 a sudden attack of pain involving the left lower quadrant of the abdomen. This was accompanied by fever, diarrhoea, urgency and frequency of micturition and burning on urination. In April, 1941 colostomy was performed for multiple polypi of the colon and for a constricting perforating lesion of the sigmoid colon. At the Mayo Clinic the diagnosis, of multiple polypoid disease of the whole colon with a sigmoido-vesical fistula from a malignant lesion, was confirmed. On 16th July, 1941 an exploratory operation was performed and the sigmoid was removed; a segment of the bladder measuring 4 by 3 inches was removed, and a drainage tube was inserted and was left in the bladder. There was an adenocarcinoma, grade I, of the sigmoid colon; the wall of the bladder was not involved in the carcinoma, but the tip of the appendix contained an adenocarcinoma, grade I. A month later fulguration of the polypi was begun by proctoscopic and sigmoidoscopic means. In January, 1942 the remaining part of the transverse colon, the splenic flexure and the descending colon was removed. The patient subsequently gained fifty pounds in weight and returned to practice in 1942.

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CONCUSSION AND COMPRESSION

See also B.E.M.P., Vol. III, p. 355; and Cumulative Supplement, Key No. 255.

Contusion

Major contusion

Acute cerebral oedema.—J. Arce, Professor Emeritus of Surgery, University of Buenos Aires, Argentine, reported before the Academy of Medicine, New York, observations made some years ago with the late M. Balado on a constant initial lesion in head injuries. The head injuries under consideration may cause haemorrhages varying in size from punctate spots to haematomas the size of hazelnuts and more or less confluent, with fluid separating the nerve cells and fibres and producing acute cerebral oedema which causes intense acute cranial hypertension and may thus prove fatal. The lesion which is constant from the time of the injury is the acute cerebral oedema. The treatment recommended is absolute rest and prompt correction of the cranial hypertension; operative intervention is not advised unless local lesions present special and urgent indications for an emergency operation. The hypertension

is reduced by the intravenous injection every eight hours of 20, 25 and 30 cubic centimetres of hypertonic saline solution of 25 per cent concentration. This treatment may be combined with decongestive purgatives. At the onset no attempt is made to find out whether or not there is a fracture of the skull—since a radiological examination necessitates disturbance of the patient—or if blood is present in the cerebrospinal fluid. The results of the above treatment are said to be good.

Treatment

Of compression

General principles.—W. Penfield and W. Cone emphasize the importance of understanding the fundamental principles involved in the care of any patient with head injury. The length of the period of unconsciousness is by far the most important single factor in prognosis. During this period the care of the patient requires first of all the maintenance of a clear airway. The patient should be transported in the prone position to avoid aspiration of fluids into the lungs; when in hospital he should be kept semi-prone and prone alternately. Mucus must be aspirated when necessary and the mouth must be kept clean. Oxygen should be given if the colour is bad. Hyperthermia with cold dry extremities should be recognized as being neurogenic in origin and the patient should be treated by taking off all the blankets and by avoiding artificial warming. If a comatose patient is restless a cause of pain should be sought; it is generally to be found in a full bladder, and catheterization will quiet the patient. Restraint should be reduced to a minimum, the best procedure is to put the patient on two mattresses on the floor. Morphine should never be used, but paraldehyde or barbiturates are occasionally necessary. Increasing intracranial pressure is indicated by one of two syndromes, namely midbrain compression or bulbar compression. The former gives rise to paralysis of the pupil on the side of the injury, to paralysis of the opposite side of the body and to unconsciousness, with development in the late stages of paralysis of the other pupil and of the other side of the body, succeeded by decerebrate rigidity and death. Bulbar compression is associated with progressive slowing of the pulse rate, with rising systolic pressure and with Cheyne-Stokes breathing going on to arrest of respiration. Increasing compression is an urgent indication for surgical intervention. For moderate degrees of compression repeated lumbar puncture is indicated. Dehydration, if thought advisable, includes restriction of fluid intake; intravenous infusions of hypertonic solutions produce very transient effects. In patients who recover from a head injury various symptoms may require attention; the most important step is diagnosis. Are the complaints organic, resulting from continued abnormality of intracranial pressure or of the general circulation, or from meningeal traction, or are they functional? Upon the answer to this question depends the treatment—medical, surgical or psychological—to be adopted. Headache due to increased pressure can be relieved by trephining, that headache due to meningeal traction is relieved by drainage of the ventricular fluid, with simultaneous introduction of air into the subdural space.

Of concussion

By dehydration.—Since 1929 L. Rogers, basing his practice on W. Trotter's teaching, has treated prolonged unconsciousness from the post-concussional state due to a closed cranial injury by measures adopted to reduce swelling of the brain, namely by dehydration. During the years 1929–40 at the Cardiff Royal Infirmary Surgical Unit 550 cases were thus treated, and he believed that he was the first to institute the practice; he points out in 1943, however, that the late C. H. Frazier of Philadelphia preceded him in 1921, and that more than 300 years ago Ambroise Paré advocated restriction of fluids, giving of purgatives, and induction of sweating for head injuries. Rogers's treatment includes the Fowler position in bed for the patient, in order to reduce intracranial venous pressure; retention enemas of 6 ounces of 30 per cent magnesium sulphate in water every six hours; freedom from constriction of the veins in the neck; and restriction of fluids so as to produce some thirst.

Post-concussional syndrome.—The post-concussional syndrome, for which J. Y. Malone introduces a new treatment, is characterized by headache, dizziness and emotional disturbances. Whatever may be its psychopathology (a disputable subject), psychogenic factors often play a part, and any treatment which hastens recovery is of value because it tends to prevent their development. Objective signs are usually absent in uncomplicated cases, with the exception that nystagmus is often observed. On the supposition that vascular disturbances are the underlying cause of the symptoms, the author has treated twelve patients with prostigmin (neostigmine), which acts as a vasodilator. The dosage was three 15-milligram (¼-grain) tablets of prostigmin bromide daily, plus an intramuscular injection of 1 cubic centimetre of 1 in 2,000 solution of prostigmin methyl sulphate (neostigmine methyl sulphate) twice weekly. The course of treatment lasted from one to seven weeks. All the twelve patients were relieved, ten completely. Restriction of fluid intake and replacement of sodium by ammonium salts are aids to recovery.

Principles of treatment in closed head injury.—D. Denny-Brown, now Professor of Neurology, Harvard Medical School, and Director of the Neurological Unit, Boston City Hospital and earlier Officer-in-Charge, Medical Division, Military Hospital (Head Injuries), England, discusses this subject. For the purpose of discussion a closed head injury is taken to be a head injury brought about without causing a break in the scalp. The importance of making this distinction is that it excludes the question of treatment of patients with scalp

wounds and with penetrating wounds of the skull, which raise an independent series of surgical problems. Since scalp wounds are usually due to the impact of some sharp-edged object, closed head injuries are sometimes spoken of as 'blunt head injuries'. The author makes it clear that head injury, even the subdivision of closed head injury, is not a single pathological or clinical entity. Thus cerebral contusion, subdural haemorrhage and extradural haemorrhage may exist either singly or in various combinations without that immediate loss of consciousness which is called 'concussion'. The most obvious phenomenon in the majority of head injuries is unconsciousness; the condition is defined in negatives: absence of consciousness and reactions and absence of memory. In coma there is lack of all reactions except the elementary corneal, tendon and flexor reflexes. 'Semi-coma' is defined as 'coma with the addition of ability to make simple reply to painful or forceful stimuli'. 'Confusion' covers the lesser degrees of loss of awareness up to and including that in which the only defect is one of loss of judgment or lack of appropriate behaviour. The treatment for coma should be given immediately after head injury occurs; in immediate traumatic coma, or in concussion of severe degree there is a great fall of blood pressure, with peripheral constriction of blood vessels lasting for from ten to thirty minutes. The stage of preliminary shock then passes off rapidly, with an increase in the pulse and respiration rates; this stage need not be alarming, and, in simple concussion, is the prelude to restlessness and semi-coma, and finally confusion leading to recovery. But certain changes are considered, namely (1) increase in coma or other signs, (2) increase in the lumbar puncture pressure and (3) progressive diminution of all signs and symptoms. The question which exercises all minds dealing with the problem of concussion is its prognosis. The author points out that, since the introduction of electroencephalography and an encephalography, it is now realized that there is a group of cases in which prolonged coma occurs with subsequent delirium and confusion, the whole disorder gradually subsiding in days or weeks; dehydration is without beneficial effect and restraint is preferable to heavy sedation over a long period. In all cases with respiratory embarrassment morphine is contra-indicated; chloral, bromide or paraldehyde should be used. With the small doses of morphine used by British surgeons the author has not seen any untoward effects.

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CONJUNCTIVA. INJURIES AND DISEASES

See also B E M.P., Vol. III, p. 365; and Cumulative Supplement, Key No. 256

Inflammation due to bacterial infection

Acute staphylococcal conjunctivitis

Report of a case.—The following case of acute staphylococcal conjunctivitis is reported by Martha B. Lyon. A woman aged thirty had been suffering for one week from conjunctivitis with phlyctenules around the corneal margin and the condition had failed to improve under treatment. She was given a sodium bichlorate wash and holocain hydrochloride and adrenaline (epinephrine) ointment, and the phlyctenules were touched with mercurochrome. Initial improvement was followed by exacerbation, and the condition a fortnight after the onset resembled inclusion-body conjunctivitis. Scrapings from the upper lid of the worse eye contained numerous Gram positive cocci and pus cells, only a few epithelial cells, but did not contain any inclusion bodies. Culture on blood agar yielded a pure growth of haemolytic *Staphylococcus aureus* which gave a positive response to the coagulase test. The test, described by Chapman, Berens, Peters and Curcio in 1934, is believed to differentiate virulent from non-virulent staphylococci. Sulphathiazole ointment, 5 per cent, was prescribed for application night and morning and sulphathiazole solution, 5 per cent, to be instilled every two hours. At her next visit a week later the patient stated that the eyes had been normal for a few days, and no trace of inflammation was evident. Five other people living in the same house as the patient did not contract the disease.

Chronic conjunctivitis

Dangers of sulphonamide treatment.—W. H. Morrison utters a warning against indiscriminate topical use of sulphathiazole and its sodium salt in ophthalmic work. He has had several patients in whom allergic conjunctivitis has followed their use. A particularly severe case was that of a woman aged sixty-three with chronic catarrhal conjunctivitis. Sodium sulphathiazole ointment, 5 per cent, in a lanolin-petrolatum base was prescribed, to be applied to the insides and margins of the lids three times a day. Hot compresses were also ordered. Three weeks later the patient returned with increased irritation of the eyes and itching and swelling of the lids. Examination revealed red boggy lids with so much surrounding oedema that the eyes were almost closed. The palpebral conjunctiva was pale and swollen and partly covered with a white film. Sulphathiazole was discontinued and cold compresses and zinc oxide ointment were applied, and in five days the eyes were normal except for slight thickening of the conjunctiva. The lanolin-petrolatum base alone was then prescribed for the right eye,

and the base plus 5 per cent sulphathiazole for the left. After four days the right eye was unchanged but a severe reaction had developed in the left, showing that sensitivity to the drug and not to the base was responsible.

Non-bacterial inflammation

Acute follicular conjunctivitis

Outbreaks of Béal's type.—Small outbreaks of acute follicular conjunctivitis resembling Béal's type occurring in San Diego and in Portland during the months July to November, 1941 and in San Francisco during December, 1941 and January, 1942 are described in a paper by M. P. Koke, who observed and treated sixty-six of the cases. The cardinal features of the disease were acute or subacute onset with profuse unilateral lacrimation, absence of exudate, severe hyperaemia of the conjunctiva, folliculosis most pronounced in the conjunctiva of the inferior fornix, enlargement and slight tenderness of the pre-auricular glands, swelling of the lids and presence of abundant leucocytes with absence of inclusion bodies or pathogenic organisms in scrapings from the conjunctiva. The probability that the disease is due to a virus was strengthened by the occurrence of cases of pneumonitis, believed to be of virus origin, in the neighbourhood at the time. Complete resolution took place from seven to twenty-one days. Superficial keratitis, a complication not previously described in Béal's disease, was observed in seven of the author's cases, appearing three to six days after the onset of the conjunctivitis. The corneal involvement induced photophobia and a sensation as of a foreign body in the eye. Slit lamp examination revealed multiple tiny discrete superficial areas of infiltration which stained with fluorescein. They were situated in the deep layers of the corneal epithelium and were diffusely scattered over the surface. In six of the seven cases the opacities cleared up in from one to three months, in one case they were present and unchanged after five months. Treatment influenced the course of the inflammation only if instituted very early, if the second eye was still unaffected when first seen the attack in it could usually be aborted by painting the conjunctiva with 1 per cent silver nitrate solution. Sulphanilamide was given internally in one case, but had no effect.

Epidemic kerato-conjunctivitis

Discovery of specific agent—M. Sanders in a preliminary report states that he has isolated a possible specific agent for epidemic kerato-conjunctivitis. Outbreaks of the disease have occurred in various parts of the world since 1890, and the last, a considerable epidemic, began in San Francisco in 1941. The clinical signs are those of acute follicular conjunctivitis with swollen and sometimes painful pre-auricular glands. In severe cases chemosis and transient pseudo-membranes may appear. The lids, especially the upper, are oedematous. The incubation period appears to be about four or five days. Differential diagnosis excludes inclusion conjunctivitis and Béal's acute follicular conjunctivitis. In the former, inclusion bodies can be demonstrated in scrapings from the conjunctiva, glandular involvement is slight and sulphonamides bring about a rapid cure. In Béal's disease the inflammation is milder and corneal complications are absent. The conjunctival scrapings in all three diseases do not show any organisms beyond an occasional saprophyte, and a virus origin is therefore presumed. Eleven cases of acute kerato-conjunctivitis, in nine of which the diagnosis seemed fairly certain, were studied by the author. When conjunctival scrapings were injected into mice some of the animals developed vague and non-specific symptoms but recovered, and transmission was successful only for at most five mouse passages. When brain emulsion from the second mouse passage was put into tissue culture and incubated for three days, the culture injected into mice caused more severe symptoms, ending in death within thirty-six hours. Cultures made at 37° C. lost their pathogenicity after the fourth passage, but those made at room temperature continued to be infective. The infective agent is probably intracellular, since ground-up tissue cultures used for inoculation yield more regular results than the supernatant fluid alone. The chief pathological change found in mice consisted of multiple small inflammatory foci scattered throughout the cerebrum and brain stem and sometimes also in the cerebellum and spinal cord. Intraconjunctival injection produced transient catarrhal conjunctivitis in two monkeys. A human volunteer who received two applications of mouse virus to the conjunctiva developed a typical attack of epidemic kerato-conjunctivitis. That the mouse disease was of virus origin was shown by the facts that routine cultures from the mouse brains and tissue cultures did not yield any organisms, that infectivity was not maintained unless living cells were present in the culture medium and that infectivity was not lost after filtration through collodion membranes. Neutralizing antibodies were demonstrated in the serum of two patients who had recovered from the disease.

EDITORIAL COMMENTARY—Commoner Causes of Conjunctivitis in General Practice

Some of the commoner causes of conjunctivitis which may be encountered in general practice are (1) *hyperaemia* due to eye-strain, a foreign body, defective elimination of waste products from the system as in so-called gout, the use of pigment for the eye-lashes (or of other facial cosmetics), lacrimal, nasal, oral or tonsillar sepsis, ingrowing eyelashes, subconjunctival concretions, exposure to tobacco or other smoke, eversion of the lower lid, subconjunctival ecchymosis, and allergy in hay-fever and phlyctenular disease; (2) *inflammation of bacterial origin*—practically any of the known bacteria may cause conjunctivitis similar in type, although specific forms are caused by the gonococcus and by the diphtheria bacillus; and (3) *inflamma-*

tion of non-bacterial origin which is found in follicular conjunctivitis, trachomatous conjunctivitis and inclusion conjunctivitis.

Under present conditions when many people are doing war work, perhaps of an unaccustomed nature, and are working and living under defective illumination and in ill-ventilated rooms, complaints of eye-strain are often heard. The condition may be accompanied by slight hyperaemia of the conjunctiva both of the globe of the eye and of the eyelids; there may be also a collection of mucus at the inner angle of the lids in the early morning, and during the day the lids feel hot and uncomfortable. The symptoms are often relieved by the instillation of several drops of an astringent solution such as $\frac{1}{2}$ grain of zinc sulphate with 5 grains of sodium chloride in one fluid ounce of water two or three times a day. If relief is not experienced within a week it is probable that an uncorrected error of refraction is present, or, if glasses are being worn, that re-examination is required. It is a fact that small uncorrected errors of refraction cause subjective symptoms of discomfort in persons working in unhealthy atmospheres which would not cause any trouble under better conditions.

A tiny foreign body concealed under the upper lid or impacted on the cornea causes hyperaemia and perhaps a muco-purulent discharge. The patient may be quite unaware of its presence. The cornea and the mucous membrane of the everted lid should always be examined while the light from an electric lamp is focused on the eye by means of a lens. If nothing is observed, it may be that the irritation is due to a slight abrasion of the cornea or to dendritic keratitis; such an abrasion is made evident by the instillation of a drop of fluorescein solution followed by a few drops of water; the abraded area then assumes a greenish colour.

While the examiner is focusing the light on the eye an ingrowing eyelash may be noted. After it has been removed with epilation forceps the patient should be warned that it will grow again. Tiny whitish concretions in the conjunctiva of the upper lid should be dug out, after cocaineization, with the point of a small knife, they may cause a considerable amount of discomfort if allowed to remain. The sudden appearance of a circumscribed red patch over the white sclerotic—subconjunctival ecchymosis—is a frequent occurrence in middle-aged people. It is rarely of clinical significance and quickly becomes absorbed with or without treatment.

Most of the known bacteria may cause conjunctivitis and may derive from oral or tonsillar sepsis. Except in the case of gonococcal and diphtheritic organisms it is immaterial to identify the species. If seen early the everted conjunctiva should be painted once with a 1 per cent solution of silver nitrate and this will often abort the inflammation; the temporary acute discomfort caused by the painting may be lessened by the instillation beforehand of several drops of a 4 per cent solution of cocaine hydrochloride; further treatment may be by zinc drops. Acute or subacute purulent conjunctivitis of bacterial origin in adults should receive immediate therapeutic attention by swabbing the everted lids with dry cotton wool and then painting the conjunctiva with a solution of silver nitrate, 2 per cent, together with the administration of one of the sulphonamides in full doses for four days, the usual precautions being taken.

Owing to the precautions taken before, during and after delivery the incidence of ophthalmia neonatorum is very small nowadays. This most serious of all ocular inflammations may be caused by any organism including the gonococcus. From the point of view of treatment it does not matter which it is. The vital point is to carry out immediate treatment without waiting for any expert advice (although that should be obtained when possible) or before the infant is sent to a hospital. The infant should be given a quarter of a half-gramme (seven and a half grains) tablet of sulphapyridine (sulphathiazole may be used as efficaciously), crushed in milk, every three hours for twenty-four hours; then the same dose every four hours for twenty-four hours; then the same dose every six hours for the next forty-eight hours. During the four days the lids must be kept free from discharge by wiping them with cotton-wool moistened with some mildly antiseptic lotion. There is certainly no objection to painting the lids occasionally with solution of silver nitrate 1 per cent or 2 per cent, but this is not considered necessary by those who have the greatest experience in the treatment of ophthalmia neonatorum.

The differential diagnosis between follicular conjunctivitis, trachomatous conjunctivitis and inclusion conjunctivitis often puzzles experts. In all of these diseases there may be enlarged follicles or bleb-like excrescences of the conjunctiva. In follicular conjunctivitis the follicles are bead-like and arranged in rows on the lower tarsal conjunctiva especially. The condition is not of serious import and will disappear in time with or without treatment; a few paintings with 1 per cent silver nitrate solution and an antiseptic lotion are indicated.

Trachomatous conjunctivitis was a scourge of the poorer classes in England fifty years ago; it is still widely prevalent in Southern Ireland, especially in convent schools. Owing to the immigration into England during the last five or six years of thousands of trachomatous Basques, Czechs, Poles and Jews from Central Europe the disease has made rapid strides and may become still more prevalent. In most cases the diagnosis must remain an ophthalmic expertise and it is to be hoped that ophthalmologists will learn to recognize the early manifestations of the disease. Any practitioner can recognize, however, the severe and long-standing cases—the ptosis due to thickening of the tarsal plate, the scarring of the upper tarsal conjunctiva, the frequent occurrence of inverted eyelids or eyelashes, and the presentation at the upper periphery of the cornea of a neovascularization or pannus, derived from superficial

conjunctival vessels. The disease is often incurable. If the practitioner cannot avoid carrying out the treatment of a trachomatous patient he may paint the eyelids with silver nitrate solution two or three times a week and give zinc drops to be used freely by the patient. The old-fashioned copper sulphate stick is highly dangerous owing to its liability to produce ulceration of the cornea. Radical removal of the disease by the operation of excision of the tarsus and diseased conjunctiva is of value in some cases, but only three or four ophthalmic surgeons in Great Britain practise it.

Inclusion conjunctivitis is a rare disease in Great Britain. In the United States of America it is recognized by bacteriological means and it is stated to be cured by the administration of sulphonamides. In any case, spontaneous cure after six months or so is the rule.—A. F. MACCALLAN.

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CONSTIPATION

See also B.E.M.P., Vol. III, p. 376.

Aetiology

Constipation and the gall-bladder

Radiological investigation.—In a paper read before the American Gastro-Enterological Association G. H. Laing, J. M. Beazell and A. C. Ivy discuss the relation between constipation and radiological abnormalities of the gall-bladder, analysing the records of 372 patients who had been subjected to a complete gastro-intestinal X-ray examination and who because of symptoms suggesting biliary disease had also undergone cholecystography. Of these patients ninety-one, or 24.4 per cent, gave a history of constipation, that is of frequent use of cathartics. Most of them had an irritable bowel which readily responded to proper management. When the cholecystograms of the constipated were compared with those of the non-constipated patients there was not any significant difference found between the two groups in respect of the proportion of plates showing imperfect visualization or gall-stones. Incomplete emptying, on the other hand, was observed with a statistically significant increase of frequency in the constipated group. This increase was common to both sexes at all ages. Thus a relation appears to exist between disturbed activity of the colon on the one hand and of the gall-bladder on the other. In the presence of a disturbed colon the gall-bladder tends to empty slowly. Whether this slow emptying predisposes to actual disease of the gall-bladder cannot be stated with certainty. Theoretically it would be expected that a gall-bladder in such case would be more prone to infection and stone-formation. Examination of the data does not, however, bear out this hypothesis. There was not any difference to be observed between the constipated and the non-constipated groups of patients in the incidence of gall-stones, and the absence of correlation between delayed emptying and imperfect visualization suggests that stasis of bile does not dispose to cholecystitis, assuming that one of the effects of infection is to interfere with concentration of contrast medium by the gall-bladder.

Breast-feeding and constipation

Opinions from various sources.—C. McNeil describes as a special type of constipation seen in breast-fed babies a condition in which bowel action does not take place for several days and then a large, soft, healthy motion is passed. The child's general health and digestion are satisfactory. The cause is anal spasm and the remedy is to pass the lubricated little finger into the anal canal. To this F. F. Chapman rejoins that an imaginary pathology has been invented to explain a non-existent disease. He protests that many perfectly healthy breast-fed babies have a bowel action only at intervals of several days. The baby thrives and the stools are soft and healthy and it is needless to worry because the child fails to conform to the adult standard of a daily action. Aperients should not be given to these babies. R. T. Smith supports Chapman, urging that a child should be allowed to perform its functions with a minimum of interference. The process of 'training' in bowel function calls forth in many children feelings of defiance, hatred and obstinacy. The normal feeling of satisfaction when the bowel is emptied naturally at its own time is replaced by the pain and discomfort associated with the administration of purgatives, enemas or suppositories. Many undesirable traits of character and various psychoneurotic symptoms have their origin in interference with the child's natural pleasures of ingestion and elimination. Evidence has been adduced to show that vaginismus, for example, may originate in this way. On the other hand J. L. Henderson agrees with McNeil that anal spasm sometimes occurs in infants. Defaecation is accompanied by straining and the spasm of the sphincter ani is readily appreciated by inserting the little finger. In the habitual type of infrequent bowel action without anal spasm treatment is not needed. When spasm is present, the lubricated little finger should be inserted daily for several days. Aperients are unnecessary. A. C. Wilson stresses the psychological dangers of interference with bowel function. He considers that any treatment savouring of violation should not be applied to the very young child unless such treatment is absolutely necessary for the child's health, and states that infrequent bowel action in a healthy baby cannot be

considered an indication. W. C. W. Nixon quotes evidence to show that vitamin B₁ deficiency in the food of breast-fed infants may lead to constipation which can be cured by giving vitamin B₁ either to the child or to its mother.

Pathogenesis

Importance of water and bile

Physiological considerations.—The control of water balance in the colon is regarded by H. Gauss as a factor of major importance in normal bowel action. The water present in the bowel is derived partly from that ingested and partly from that secreted into the gut, probably amounting to from 2 to 10 litres per day. The colon varies in different individuals in its capacity to absorb water. Excessive absorption leaves the stool hard and dry. The normal stool contains about 80 per cent of water. It is probable that bile is the substance which determines the amount of residual water in the stool. It is not known how much bile is secreted daily, but the quantity is assumed to be between 600 and 900 cubic centimetres. If the bile exerts an osmotic influence tending to retain water in the stool it is easy to understand why diseases of the biliary system in which the flow of bile is reduced are usually associated with constipation. It has also been suggested that bile stimulates peristalsis and is thus necessary for the normal function of the intestine. The type of impaired bowel action associated with deficiency of bile is known as biliary constipation. It tends to occur in cases of cholelithiasis, cholecystitis and other disorders in which bile secretion may be supposed to be deficient. It is more frequent in women of middle age and the symptoms are a mixture of gall-bladder dyspepsia and the spastic colon syndrome. Radiography frequently reveals some pathological condition of the gall-bladder. The only satisfactory treatment is to give bile or bile salts. The optimal dose must be found by a process of trial and error. Too large a dose will cause diarrhoea and colic. It is best to begin with a small dose of a suitable preparation and increase it if necessary.

Treatment

Hemicellulose hydrogels

Effect on the bulk of stools.—R. Bauer has studied the effect of hemicellulose hydrogels upon the character of the stools. These bodies are acted upon by the intestinal bacteria, especially the *Bacterium coli*, with the production of volatile fatty acids to which the laxative effects of the hemicelluloses have been thought to be largely due. The product studied by the author consisted of granules containing hemicellulose 37.5 per cent, cellulose 7 per cent, starch, fat, minerals and water. Experiments were first made to determine whether or not hemicellulose when incubated with a normal stool for thirty-six hours produces significant quantities of fatty acids. It was found that the volatile fatty acid content of the mixture increased by about 200 per cent. Control experiments showed that the fatty acid content of the normal stool incubated without the hydrogel product increased by only 50 per cent. When the product was administered daily to six patients on a standard diet the total quantity of volatile fatty acids passed in the stools was considerably increased, owing partly to a moderate increase in the percentage present in the stool, chiefly to the great increase in the bulk of the stools. The water content of the stools was much increased although the consistency remained semi-solid. This is probably due to the ability of hemicellulose to absorb more than ten times its weight of water. The stools contained little free acid, the reaction to litmus never being acid. Although increased in amount, the volatile fatty acids were at no time thought to be enough by themselves to produce a laxative effect; but it is possible that when reinforced by the water-binding action of the unchanged moiety of the hydrogel they are able to do so. Volatile fatty acids when administered orally have to be given in very large doses before a laxative effect is apparent.

Use of phenolphthalein

Non-irritant effects on bowel musculature.—P. Blick, J. B. Berardi and O. Wozasek have studied the action of phenolphthalein in dogs, with a view to determining its mode of action and finding whether or not it has an irritant effect on the bowel. When doses of 0.5 to 1 gramme (8 to 15 grains) were introduced directly into isolated loops of intestine, subsequent examination of the contents of the loop did not reveal any of the products of irritation (leucocytes, mucus or protein). Intravenous injection increased the peristaltic activity of the colon. The drug appears to act directly on the musculature of the bowel; its action is not abolished by atropine which paralyses the motor nerves of the intestine. When given by intravenous injection, it has not any effect upon the blood pressure and electrocardiogram, that is upon the parasympathetic nervous system.

The rush to aperients

Need for simple hygienic routine.—R. Coope expresses the hope that the shortage of drugs due to war conditions will do something to check the widespread abuse of aperients. Liquid paraffin and phenolphthalein are already in short supply. Many people use aperients as a substitute for sane living. Regular action of the bowels is best insured by plenty of work and exercise; plenty of good simple food, bulk being most important; sufficient fluid; and a sensible outlook. Many people are finding bowel action facilitated by the natural laxative action of the present wholemeal bread. Too many practitioners are content to humour rather than to educate their patients.

EDITORIAL COMMENTARY—The Management of Dyschezia

All cases of constipation can be separated into two groups: colonic constipation, in which the passage through the colon is delayed, and dyschezia, in which the faeces reach the rectum at the normal rate but final evacuation is delayed owing to inefficient defaecation. Dyschezia often originates in neglect to respond to the call to defaecate owing to laziness, insanitary conditions of the water-closet or false modesty. The rectum dilates so that an increasing quantity of faeces is required to attain the adequate internal pressure necessary to produce the call to defaecate and finally the sensation is lost completely. The patient, however, is still capable of emptying his rectum if he tries, but by now he has generally convinced himself that he cannot get his bowels opened unless he takes a sufficient dose of aperient to produce fluid faeces which require no effort for their evacuation. Dyschezia may also result from weakness of the voluntary muscles of defaecation, the assumption of an unsuitable posture during defaecation, and in diseases of the anal canal voluntary inhibition from fear of pain. But whatever the primary cause, the final result is the same. The defaecation reflex is lost, and the incomplete evacuation results in the accumulation of faeces in the rectum.

In dyschezia the retention of solid faeces in the rectum, which is normally empty except immediately before defaecation, may give rise to a number of reflex symptoms, such as headache and general malaise, which disappear directly the bowels are opened. The instantaneous relief proves that these symptoms are not caused by auto-intoxication. Moreover, experimental distension of the rectum with a large plug of wool produced identical symptoms. The pressure on the surrounding parts by the retained faeces also gives rise to perineal discomfort. Pressure on the haemorrhoidal veins may be the exciting cause of haemorrhoids, and the passage of large hard scybala through the anal canal may produce an anal ulcer. The majority of patients consult a doctor only after they have begun to treat themselves with aperients. They regard themselves as constipated because they take aperients, although frequently their bowels would act sufficiently without artificial aid. The patient should therefore be instructed not to take any aperient and to make an effort to open his bowels every morning after breakfast, even if he feels no inclination to do so. He generally succeeds and it is then clear that he is not constipated at all and that both the local and general symptoms of which he complains are the result of purgation. If, on the other hand, the bowels are not opened, the abdomen and rectum should be re-examined; an empty colon and a full rectum indicate the presence of uncomplicated dyschezia. If the rectum is empty and if hard scybala can be felt in the pelvic colon through the anterior rectal wall, pelvic colon dyschezia is present. In the rare cases in which both the pelvic colon and rectum are empty, it must be assumed that the more proximal part of the colon is at fault. In severe cases the diagnosis should be confirmed and amplified by an X-ray examination, carried out during a period in which the patient is not taking any aperient, and after an opaque meal has been given. In dyschezia the passage through the colon is found to be at the normal rate or even more rapid than normal, all the barium sulphate collecting in the rectum or rectum and pelvic colon in twenty-four hours.

Dyschezia can be cured by restoring to activity the defaecation reflexes, which have been allowed to become inefficient by neglect or by interference with their normal performance by the habitual use of aperients. A simple explanation of the physiology of defaecation and encouragement are often all that is required, but it may be necessary to reduce the work the muscles of defaecation have to perform by giving once or twice a day a teaspoonful of an unabsorbable vegetable mucilage such as I-so-gel or a dessertspoonful or tablespoonful of liquid paraffin in order to soften and increase the bulk of the faeces. The patient should be instructed to take salad or cooked green vegetables once or twice a day, and fruit—raw, stewed or as jam—as often as possible.

If the patient is quite unable to evacuate his rectum although it is loaded with faeces, an enema of one fluid ounce of glycerin should be given in the morning after an unsuccessful effort has been made. The strength of the enema should be gradually reduced by replacing one fluid drachm of glycerin by water every other day until only water is used. By this time the normal defaecation reflex and with it the tone and contractile power of the rectum have almost invariably returned. Alternatively a pint of plain water can be used instead of glycerin, and the bulk reduced by two fluid ounces every day until the smallest effective quantity is found. This should be given every third day if the bowels have not been open in spite of an unhurried effort after breakfast each morning. Within a month the defaecation reflex is generally restored and enemas are no longer required.—ARTHUR HURST.

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CORNEA, INJURIES AND DISEASES

See also B.E.M.P., Vol. III, p. 424; and Cumulative Supplement, Key No. 260.

Injuries*Chemical injuries*

Keratitis due to phosphorus.—T. K. Lyle and A. G. Cross report a case of sclero-keratitis following phosphorus injury of the eye. The patient, an airman aged forty-three, served in the Royal Flying Corps in the war of 1914–18; in 1918 he was handling a barrel of phosphorus when it exploded, causing burns of the face, eyes and body; he was admitted to hospital and apparently recovered. From that time onwards he suffered from recurrent attacks of redness and pain in the eyes and with photophobia; the last attack started in 1941 and continued until he came under observation. The authors point out that the history resembles that of mustard-gas keratitis but that the clinical features were different. The main lesion was scleritis, and the eye did not show any evidence of past corneal ulceration, the corneal scars being deep in the substantia propria and not coalescing with the sclera; the irregular vascularization seen in gas keratitis was absent; and evidence of uveitis was not apparent.

Gas injuries in warfare

Mustard-gas keratitis.—T. L. de Courcy has had a case of mustard-gas keratitis under close observation for twenty years. The patient, a man now aged sixty-two, served in the war of 1914–18 and before that he was a county tennis player. In May 1918 he was close to a bursting gas shell and thinks that some of the liquid entered his eyes. He was treated for acute gas poisoning, and three months later was passed by a medical board and returned to France, but he asked the board to note that his sight was less good than before. On demobilization he repeated that he was still not seeing so well and again came before a medical board, when he was told that his eyes really had suffered as the result of gassing and he was granted a 15 per cent pension. He consulted the author in 1922 because he could not stand the light and found that his golf and tennis were suffering. At that time slight scarring of the corneas and a small degree of hypermetropic astigmatism were noted. The astigmatism progressed rapidly during the next three years, and gradually became of mixed type. In 1924 it was noted that both corneas were anaesthetic; in 1925 the patient had an attack of ulceration in the right eye, in 1926 in the left eye, and attacks continued to recur at intervals of not more than a year until 1937. Each attack left scars which gradually so much reduced the vision of the right eye that in 1928 attempts to improve vision by glasses were abandoned. Until 1938 he was able to read with the left eye by holding the book close to the eye. Slit lamp examination in the latter part of the period 1920–30 showed that crystals were present in the substance of the cornea; they have gradually disappeared. Vascularization of the cornea was present from the early stages. The ulcers in the early days were treated with caustics and other remedies, but showed so little improvement under this regime that saline and oily solutions were substituted. On several occasions tarsorrhaphy was done but ulceration recurred as soon as the lids were opened. X-ray therapy was tried in 1936 and appeared to cut short an attack of ulceration. Short-wave diathermy has apparently prevented any ulceration since 1937. A contact lens has enormously improved the vision of the left eye; it is now 6/9 and newspaper type can be read comfortably. Cauterization of the blood vessels at the limbus has also been carried out with good results. The patient leads an almost normal social and business life.

Ulcers*Sequels to ulceration*

Lenticular changes.—B. Samuels, in a paper read before the American Ophthalmological Society, describes the lenticular changes occurring after healing of perforating corneal ulcers as he observed them. The material studied consisted of thirty-six globes, removed by operation, in which a corneal scar had been present for periods ranging from several months to fifty years. Many of the lenses were severely damaged. Ten had become transformed into membranous cataracts, seven were adherent to the cornea. In nine lenses the cortical substance seemed to be entirely fluid. Three showed Morgagnian cataracts. Four showed extensive calcareous degeneration, in the form of an inverted shallow saucer lying in the anterior and equatorial cortical substance. Ossification was noted in one case. In one globe spontaneous expulsion of the calcified lens was seen in the act of taking place. Rents in the capsule had resulted in several instances in the hour-glass formation known as Soemmering's crystalline swelling. Separation and folding of the capsule was common. Proliferation of the subcapsular epithelium was often present. In one case proliferated lens epithelium was found outside the lens capsule and entirely independent of it. It is suggested that this represents an abortive attempt at regeneration of the lens. Four dead lenses were encountered.

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CRANIAL NERVE AFFECTIONS

See also B.E.M.P., Vol. III, p. 470.

The eighth nerve*The cochlear division*

Discussion of tinnitus aurium.—E. P. Fowler draws a distinction between the two forms of tinnitus: vibratory, caused by autogenous vibrations reaching the ear from any part of the body, and non-vibratory, caused by some biochemical irritation. Successful treatment depends upon recognition of the type involved. The amount of annoyance caused by the vibratory form depends largely on the psychological reactions of the patient; the sound is a real sound and can therefore as a rule be readily rationalized. Treatment is primarily a matter of psychotherapy. In the non-vibratory form the sensation is not caused by actual sound. It seems unnatural, and like all illusions tends to be exaggerated. Conditions which may be associated with this form of tinnitus are as follows: impacted wax; pathological closure of the pharyngeal (Eustachian) tube; traumatic lesions of the inner ear; otitis media and otosclerosis; the effect of drugs such as quinine, salicylates, arsenic, sulphonamides; cardiovascular disorders; gastrointestinal disturbances; psychoneurosis; allergy; idiosyncrasy; lesions of the otic, gasserian or geniculate ganglion; and intracranial growths. The mode of action of these various factors is probably directly or indirectly upon the blood supply to the auditory neural elements or their supporting tissues. This may be supposed to result in partial anoxia followed by oedema. The ideal to be aimed at in treatment is removal of the cause. If this is impossible relief can sometimes be given by vasodilators such as glyceryl trinitrate (nitroglycerin). Should the condition prove intractable the best hope lies in improving as far as possible the patient's outlook and mental attitude to his complaint.

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DEAFNESS

See also B E M.P., Vol. III, p. 555; and Cumulative Supplement, Key No. 284.

Anatomy of the ear*Mechanism of hearing*

Physiological survey of the conducting apparatus —F. C. Ormerod in his presidential address to the Section of Otology of the Royal Society of Medicine discusses the advances which have been made in the study of hearing during the last two decades. He points out that in its analytical powers the ear is unrivalled by any other sense organ and that this discriminating faculty necessitates a complicated receptive mechanism. The conducting apparatus includes the following. (1) The tympanic membrane, capable of being set in vibration by sound waves of exceedingly minute intensity, the ossicles have been seen by means of a low power otomicroscope with a stroboscopic attachment to respond to a stimulating tone of 128 cycles of an intensity of 75 decibels or over. (2) The ossicles, which move in and out as one mass, the movements of the malleus and incus are solely in and out about an axis which corresponds within one-hundredth of a centimetre to the centre of gravity of the malleo-incudal mass; the stapes has a rocking movement; with considerable degrees of movement its excursion is said to change to a rotation about the long axis of the footplate which imparts considerably less energy to the endolymph of the cochlea and must be regarded as a protective device. (3) The intrinsic muscles, which modify the movements of the ossicles, an association exists between the orbicularis oculis and the stapedius, shown by the drumming in the ears which can be produced by strong voluntary contraction of the orbicularis oculis; the stapedius appears to act as a brake on the stapes and seems to prevent excessive excursion of the footplate through the oval window; evidence has been obtained that the muscles exert a damping effect on low tones which is not only protective but which also improves hearing at higher pitches. (4) The windows, which are probably both responsible for conducting sound to the cochlea by different routes, it has been suggested that sounds of low pitch are conducted by the ossiculo-cochlear route by way of the oval window and sounds of high pitch by the acro-cochlear route by way of the round window, normally the former route is the more important. Bone conduction plays an important part in hearing, vibrations being transmitted to the ossicles through the movements of the bones of the skull or by bony trabeculae. Auditory fatigue is produced chiefly by stimuli above 1,000 cycles. It probably has a central basis. Localization of sound depends upon ability to recognize differences of intensity, phase or time of arrival of sound.

Types of deafness*Deafness without obvious cause*

Testing of the 'hard of hearing'.—The Winthrop Foundation for the Study of Deafness was established at the Massachusetts Eye and Ear Infirmary in 1940. An account of the work done in connexion with the 'hard of hearing' whose deafness was not due to any obvious disease of the ear is given by W. Mueller, who describes the method of examination practised by him in more than 500 such patients. The auricle and external meatus were first inspected and the presence or absence of the cough reflex and of cerumen was noted. The appearance of the tympanic membrane and the discernibility of the middle ear structures were observed. The mobility of the tympanic membrane and of the malleus was tested by means of the Siegle-Brünnings pneumatic otoscope. The Gellé test was carried out. The patency of the Eustachian tubes was tested by Politzer's method: if the tubes did not open when the patient uttered the sound 'kay' he was asked to swallow air, and if this was ineffective he was given water to swallow. If the tubes still refused to open, catheterization was employed after the examination

had been completed. Failure of the tubes to open appeared to be due in many cases to operative damage to the soft palate. Examination of the nose was carried out, followed, if the findings warranted it, by X-ray examination of the accessory sinuses. If the inferior meatuses of the nose were wide enough to admit the Holmes nasopharyngoscope, the Eustachian tube orifices were examined with this instrument, after application of a local anaesthetic, pontocaine hydrochloride (butethanol, Decicain). The postnasal mirror was used to examine the vault, posterior wall and lateral recesses of the pharynx, after application of pontocaine. The teeth were examined and X-rays taken if this appeared advisable. The fauces and posterior pharyngeal wall were inspected. Audiometric tests adapted to different age levels were performed. Down to the age of about three and a half years the tests used were as follows. pure tone audiometer for both air and bone conduction; ditto with phonograph attachment for testing with words; Weber test; Rinne test. The Gellé test had already been carried out during the general examination. In children under three and a half years a 'play-conditioning' technique was employed. This method involves the use of bells, rattles, whistles, and other sound-producing objects, to which the child responds by activating various toys. The treatment recommended included insufflation, tonsillectomy and X-ray treatment of the pharynx and Eustachian tubes, and in selected cases fenestration operations.

Treatment

Otosclerosis

Analysis of surgical methods.—The results of various surgical operations designed to improve hearing in otosclerosis are critically examined by G. F. Shambaugh, Jun. The lesion which is primarily the cause of deafness in this disease is fixation of the stapes, and the aim of surgery is to construct a new window into the labyrinth to replace the occluded oval window. Experience has shown that when hearing by air conduction is forty to sixty decibels lower than hearing by bone conduction the fixation of the stapes may be regarded as complete, and the case as one suitable for operation. Once the stapes is fixed, variations in the degree of deafness are due to secondary nerve degeneration, which is unaffected by operation. For comparison of the results of different surgical procedures certain criteria must be satisfied. Every case should be reported. Hearing for speech should be measured audiometrically and recorded before and after operation for both ears. The ear which is not operated upon then furnishes a control. All audiograms should be made under comparable conditions. Because of the normal variations in hearing in untreated otosclerosis a change for speech of less than ten decibels must be disregarded. The author's experience is that at least six months must elapse before regarding the result of fenestration as permanent; any case reported under six months is not worth considering. All complications and disasters should be recorded. Care must be taken in selecting cases for operation to include only those with primary ankylosis of the stapes and to exclude other kinds of deafness such as that resulting from secretory otitis secondary to tubal obstruction. The author's analysis relates to the following methods of operation. (1) The original Lempert fenestration operation (fifteen ears). (2) The Lempert technique with the addition of a device providing for a continuous flow of normal saline across the horizontal canal during the making of the fistula, to wash away all blood and particles of bone (thirty ears). (3) The further addition of a binocular dissecting microscope to facilitate the making of the fistula (sixty-six ears). (4) Lempert's 'nov-ovalis' technique modified by continuous irrigation and the use of the microscope (seventy-two ears). The site of the nov-ovalis fenestra, stated by Lempert to be the 'dome of the vestibule', is according to the author more accurately described as the anterior part of the ampulla of the horizontal semicircular canal. The audiometric results of these four procedures were as follows: lasting significant improvement in hearing was obtained by the first method in 27 per cent of cases, by the second method in 76 per cent, by the third method in 78 per cent; by the fourth method in 88 per cent. The author utters the warning that as the new window is larger when made by the nov-ovalis technique, bony closure may be a slower process and that therefore six months is possibly not enough to allow when assessing the results of operation. Not a single death occurred in this series and the only complication met with has been one case of facial paralysis lasting for two weeks after operation.

Preventive and palliative methods.—F. T. Hill emphasizes the fact that chronic progressive, so-called catarrhal, deafness (otosclerosis) is an incurable disease. Treatment, once the condition is fully established, can be palliative only; prevention is therefore of the utmost importance, and careful audiometric tests for all school children with proper subsequent medical supervision of any found to be deficient are advocated. Theories of causation include negative pressure due to obstruction of the Eustachian tube; toxic absorption resulting from focal sepsis; endocrine and nutritional deficiencies. If evidence of tubal obstruction, of which diminution of hearing for the higher frequencies is most reliable, is obtained, the cause should be sought and will usually be found in the sinuses or the nasopharynx. X-ray treatment may be successful in destroying hypertrophied lymphoid tissue in and about the Eustachian tube, and is of special value as a preventive of deafness in children. Insufflation of the middle ear is often helpful but should not be employed as a routine measure without an attempt to find and remove the cause of the tubal block. Foci of sepsis should be eliminated and general health improved, but these measures are of more value from the preventive than from the therapeutic point of view. Many attempts have been made to overcome by surgical operation obstacles which prevent the sound-waves from reaching the inner ear. Various procedures

including myringotomy, removal of ossicles and trephining of the labyrinth have been tried, but with the exception of fenestration they have fallen into desuetude. So far as the operation of fenestration is concerned, claims have been advanced of recent years, but it must be regarded as still on its trial and should be used only for selected patients. For most cases of chronic progressive deafness a suitable hearing aid is the best form of treatment. The patient must be helped to cultivate a cheerful outlook and to adjust himself to his difficulties.

EDITORIAL COMMENTARY --The Meaning of Noises in the Ears

Tinnitus aurium is a variable complex symptom for which there is no apparent objective explanation. It is described by patients as a hissing, buzzing, ringing sound, a throbbing noise and even as the sound of voices. The last is, however, an auditory hallucination associated with mental disease. There is one rare form of tinnitus resembling the tick of a clock, and this can be heard by the observer with an auscultating tube as well as by the patient. It is produced by the rhythmical contraction of the pharyngeal muscles, a spasmodic tic sometimes seen after encephalitis lethargica. Alternatively it may be a habit spasm. The character of the tinnitus does not give any clue to its pathology. The throbbing and rhythmical variety is said to be of circulatory origin. The majority of patients state that they do not hear the noise when they are occupied in doing something which commands their full attention and that the noise does not prevent sleep. However, a few severe cases of tinnitus with mental upset affirm that the roaring noise is always present and drives them to desperation.

The onset is often sudden. The patient realizes suddenly that the noise is in his own ear and does not arise from some outside appliance such as a gas jet. In a large group of patients the tinnitus is of central origin and no objective signs of any kind can be found elsewhere. This type is represented by the highly strung neurasthenic woman at the menopause or after hysterectomy in which examination does not reveal any physical signs. The ear-drums, hearing, Eustachian tubes, nose, throat and nasal sinuses (including the sphenoidal sinuses) are all normal. The blood count, blood pressure and optic disks are also normal. Some old people with arteriosclerosis suffer from intractable tinnitus, but it is overshadowed by other symptoms of arteriosclerosis.

I have never found a septic focus associated with tinnitus, but intestinal auto-intoxication as the result of constipation was considered by our predecessors to be a frequent cause and they always commenced treatment by giving doses of calomel. Tinnitus after the administration of quinine and salicylates is often temporary and is rarely noted. The chronic alcoholic prefers to accept the noises in his ears rather than give up alcohol. Tinnitus is a symptom in certain diseases of the central nervous system such as tumours and lesions of the posterior fossa. In a small proportion of cases it is an aura of epilepsy and may be associated with migraine. When the ear is responsible for the tinnitus in the early stages the symptom and the ear disease are unilateral. It is accepted that either the cochlea, the auditory nerve or the temporo-sphenoidal lobe is the source of the symptom.

There are certain conditions of the ear which are associated with tinnitus. It is a pity that a simple condition such as the presence of cerumen as a cause is rare; the cessation of the tinnitus by removal of the wax is gratifying. Tinnitus is a constant symptom in Ménière's triad of symptoms or syndrome: vertigo, deafness and tinnitus. It is constant in cases of acoustic nerve tumour. It is also a diagnostic symptom of otosclerosis which is a degeneration of the nerve ending in the cochlea. The tinnitus of otosclerosis is difficult to treat with success and there is not any drug which has the slightest effect. As the deafness increases, the tinnitus decreases. The tinnitus of secondary sclerosis occurring after otitis media is similar to otosclerosis, that is the sclerosis has extended to the cochlea. Eustachian obstruction can produce tinnitus but it is uncommon and is probably a contributory cause only. Patients with tinnitus respond very quickly to the caloric tests showing that the semicircular canals are not affected.

The first step in treatment is to ease the patient's mind and as far as possible to give a hopeful prognosis. An effort should be made to induce the patient to ignore the noise and in some cases, by reassurance, abolish the fear of insanity. Anything which causes or aggravates the condition should be eliminated. Continued loud noises, fatigue and alcohol are important contributory causes. Any condition of the ear likely to be a cause is treated, but otherwise the ears should be left alone.

The treatment of the general condition of the patient is of the greatest importance. Many drugs such as hydrobromic acid, bromides and phenacetin have had periods of popularity but small doses of codeine and phenacetin are the most successful. When the blood pressure is low, ephedrine by the mouth in the form of the elixir ephedrinae hydrochloridi (B.P.C.), ergotin or prostigmin have been tried. When the blood pressure is high bellafoline (Sandoz) has been prescribed. Any drug which suddenly increases the blood pressure will increase the tinnitus. Furstenberg's sodium-free diet has not been successful and very few patients will tolerate such a diet.

Operations for the division of the auditory nerve and for the destruction of the cochlea have been done in extreme cases without success. Dandy divided the auditory nerve for the relief of vertigo in cases of Ménière's syndrome of forty-two patients. The tinnitus persisted in 50 per cent of these cases. I have destroyed the cochlea on several occasions but the tinnitus has always persisted. The result of the division of the auditory nerve indicates that the site of the lesion is central to the point of section of the nerve in some cases. Lumbar puncture

or the reduction of intracranial pressure by hypotonic solutions given intravenously have been unsuccessful. Ligature of the carotid artery or even compression is dangerous and has not relieved the symptom. Anaesthetization of the spheno-palatine ganglion by the injection of novocain (procaine hydrochloride) has failed. Cervical sympathectomy with removal of the stellate ganglion on both sides of the neck has been done and success claimed, but the number of cases of this operation is too small to justify a conclusion. The operation which has had the most success is division of the auditory nerve. Only a small minority of patients with tinnitus will consent to an operation.

It will be gathered from the above that every case of tinnitus requires a complete and thorough examination both general and local, followed by appropriate and prolonged treatment. Operative treatment is justified only when other treatment has failed and the tinnitus is intolerable.—EDWARD D. D. DAVIS.

Hill, F. T. (1942) *Ann. Otol., etc., St. Louis*, **51**, 653.

Mueller, W. (1942) *Ann. Otol., etc., St. Louis*, **51**, 756.

Ormerod, F. C. (1943) *J. Laryng.*, **58**, 1.

Shambaugh, G. E., Jun. (1942) *Ann. Otol., etc., St. Louis*, **51**, 817.

DENTAL SEPSIS IN RELATION TO SYSTEMIC DISEASE

See also B L.M P., Vol III, p. 596, and Cumulative Supplement, Key No 288.

Dental disease in children

Care of school children's teeth

The situation in South Australia.—Marjorie C. Smith addressed the Medical Sciences Club of South Australia on the subject of the efforts made by the South Australian Education Department in connexion with school children's teeth. Every child has a medical examination during the first year at school, and four further examinations are made at intervals during school life. When dental caries is found a notice is sent asking the parents to take the child to a dentist, and to unemployed parents an order for the Dental Hospital is also sent. The whole responsibility for obtaining treatment thus rests with the parents. In country districts the school dentists visit schools and treat free of cost all children whose parents consent and cannot pay for dental treatment. Each district can be visited only once in three years, a most unsatisfactory arrangement for both dentists and patients. In Adelaide in the last two years an average of 63 per cent of the children examined had dental trouble and in most cases it was serious. In children over twelve it is rare to find only one tooth which needs to be attended to. Frequently by the time the child goes to high school the upper incisors are badly decayed or are absent and some children already have double sets of dentures. The causes of this state of affairs are ignorance and poverty. The Department is carrying on an educational campaign. Teachers are instructed to hold tooth-brush drill and to give lessons on the care of the teeth. Talks are given to mothers' clubs and instruction has been broadcast. Lack of money to pay for dental treatment is a problem in many poor homes. In war-time, with higher wages and free treatment for the families of men in the Forces, things are easier but many poor families are still unable to obtain treatment. More hospitals are needed, and 'flying dentists' who can visit people in remote districts are essentially required.

Dental hypoplasia and caries

Dietary deficiency as the basis.—The relation between hypoplasia of the teeth and dental caries has been investigated by J. Staz. Of a group of seventy-three Indian children attending a private school in Johannesburg, thirty-nine were found to show hypoplastic teeth. Of the thirty-nine cases of hypoplasia three were of the local and thirty-six of the general type. The number of teeth without any hypoplasia was 1,388, with general hypoplasia 299 and with local hypoplasia three. Eighty-five of the 302 hypoplastic teeth belonged to the deciduous series and 217 were permanent teeth. The smallest number of hypoplastic teeth in any one child was one, the largest number twenty-four. The average age of the children was just over eight years; forty-three were boys. Three children only had a history of rickets and one of these children had normal teeth. The largest average number of hypoplastic teeth occurred in the children with a history of exanthematous disease. The children had been brought up on strictly vegetarian lines and it is probable that the diet during the developmental stages of tooth formation was often deficient, especially in lime salts and vitamin D. Several of them were in the habit of eating large quantities of sweets. It is considered likely that dietary deficiency was the chief factor retarding development of the teeth, with an acute illness as an adjuvant factor in many cases. Examination for dental caries gave the following results. Of the thirty-four children without dental hypoplasia twenty-four showed caries, the number of cavities per mouth ranging from one (six children) to twenty-nine (one child), with an average of 5.1. Of the thirty-nine children with hypoplastic teeth twenty-six showed dental caries. The number of cavities in each mouth ranged from one (five children) to twenty-seven (one child), with an average of 3.5. The total number of carious hypoplastic teeth was thirty, and the average number of cavities per hypoplastic tooth was 0.1. The total number of normally developed carious teeth was 208 and the average number of cavities per normally developed tooth was 0.2. It is thus seen that in this group of children the incidence of caries in normally developed teeth is double that in hypoplastic teeth. This is contrary to the view that a tooth showing defective development is more susceptible to dental caries than is a normal tooth.

Malnutrition and dental development

Need for education of the people.—An Editorial in the *American Journal of Orthodontics and Oral Surgery* draws attention to the relation between malnutrition in children and the development of the teeth. The study of nutrition has been one of the outstanding contributions of Medicine to public health. Malnutrition does not necessarily imply deficiency of some essential element. It is a matter of imbalance, and excess may be equally harmful. In the case of fluorine, for example, the presence of too much of this substance leads to unsightly discoloration of the dental enamel just as too little results in imperfect formation. Malnutrition in childhood is far more prevalent and more detrimental to growth and development than is generally realized, and its correction requires careful preliminary study. The dentist who considers that a child is inadequately nourished should not be content merely to prescribe orange juice and calcium. Once a child has deviated from the normal he tends to continue to run on a wrong course, and to bring him back to normal is a matter for one who has thoroughly studied the subject of nutrition. Unintelligent selection and improper preparation of food, an insufficient intake of milk, repeated infections, allergy and so on, all have to be taken into account. Orthodontists are awakening to the importance of nutritive factors and are becoming increasingly reluctant to correct malocclusion in children whose general nutritional condition is unsatisfactory. Such children are recognized by their tired, pale appearance and lack of fatty tissue, especially about the neck, chest and thighs. The state of the mouth and teeth offers further evidence of unsatisfactory feeding. The Canadian Council on Nutrition planned a programme covering the whole of 1943 and designed to educate the public in the importance of proper feeding. It is to be hoped that further investigation will reduce the incidence of malocclusion and dental troubles in children.

EDITORIAL COMMENTARY—The Importance of the Deciduous Dentition

There is a very common belief that a child's temporary teeth are of little importance because they will all fall out after a short period of usefulness. There is no difficulty in showing why this idea is wrong and harmful, but by the time dental surgeons have been consulted and have had the opportunity to explain and instruct, much damage has often been done. It is very desirable therefore that medical practitioners should cooperate as fully as possible in this preventive work.

The evils of early decay and loss of the deciduous teeth may be considered under three heads: (1) loss of masticatory efficiency; (2) toxæmia from a septic mouth; (3) irregularities in alignment of the permanent teeth. The day has fortunately passed when children up to five or more years of age are fed on soft and pappy foods, and the pendulum has perhaps swung almost too far the other way, but the molar teeth of a child of three years of age are there for a purpose, and should obviously be fully used in the comminution of simple normal food-stuffs. If the two temporary molars on each side of each jaw be compared with the two permanent molars and the two premolars at the age of about eighteen, it will be found that the masticating area is considerably greater in relation to body weight at the earlier age. These teeth serve the child until he reaches the age of six, when the first permanent molars erupt at the back of the jaws. Then follows the process of transition, between the ages of six and twelve, which is so effectually spaced and timed that never for any period is the child's masticatory efficiency really impaired. After the changes in the front of the mouth, the temporary molars are replaced by the premolars, and the permanent canines lock the arch, without any disturbance of function. At twelve years of age the second permanent molars erupt at the back of the jaws, which in the meantime have been growing sufficiently to accommodate them, and except for the wisdom teeth the process is complete. It stands to reason that for a growing child the capacity to deal thoroughly with the constituents of a normal diet is of even more importance than for an adult. The one factor which commonly inhibits this ability is dental caries, which, in many cases, induced by errors in diet, has become rampant in children as young as four years of age. It is not generally appreciated that tenderness of a tooth on one side of the mouth puts that side out of commission, and that if this happens on both sides the child quickly acquires the habit of bolting his food, thereby causing digestive troubles and malnutrition. The premature loss of the temporary molars—especially the second, which are much larger teeth than the first, and for most of the period of their existence are located in that part of the jaw (about half-way between the front and back) at which mechanical efficiency is at the maximum—although it does not necessarily throw one side out of action, must necessarily impair function. It should be remembered that the loss of one tooth reduces total efficiency by about one-quarter, because the opposing tooth (or teeth) is rendered useless. If a serious loss of temporary teeth has occurred by the time the child is about four years of age he is unable to masticate properly until the eruption of the first permanent molars at the age of six to seven, and even then these teeth are located too far back in the jaw for maximum mechanical efficiency. Loss of temporary teeth after the eruption of the first permanent molars may be almost as disastrous, because the second temporary molars in particular should function until about the age of eleven.

It is not necessary at the present time to stress the evil consequences of dental or oral sepsis, both near and remote. In the case of children, sepsis exaggerates the malnutrition caused by lack of masticating efficiency, and growth and development are inhibited. Absence of teeth is an evil lesser than that of septic teeth. The first principle of treatment should be to prevent

caries by diet; the second should be to preserve teeth by treatment when this has failed; and the third should be to eliminate sepsis, when both have been unsuccessful.

Premature loss of teeth brings further evils in its train. In the normal process of succession there is only a short period between the loss of a temporary tooth and the eruption of its successor, but when the temporary tooth is lost early the adjacent teeth tend to approximate, so that insufficient space is retained for the successor, which may erupt outside or inside the arch, and there may be a flattening of the arch. In severe cases of early loss of temporary teeth there may be a collapse of the arch and a high degree of irregularity of the permanent dentition. The most important teeth for retention for the full natural period are the second temporary molars, especially the upper ones, because when these are lost prematurely the permanent molars either move forward or tilt. The result of this is insufficient space for the second premolars and canines. Prominence of the upper canines placed outside the arch is also often caused in this way. Irregularity of the dental arches must not be regarded as of aesthetic importance only; it renders function less efficient, and the misplaced teeth are made more liable to dental caries — NORMAN BENNETT.

Editorial (1943) *Amer. J. Orthodont. oral Surg.*, **29**, 170.

Smith, Marjorie C. (1942) *Med. J. Aust.*, **2**, 269.

Staz, J. (1943) *S. Afr. med. J.*, **17**, 1.

DENTITION

See also B.F.M.P., Vol. III, p. 603.

Disorders associated with dentition

Analysis of one hundred consecutive cases

Summary of conditions found—Pointing out that such disorders are often misinterpreted as 'teething', D. Paterson analyses 100 consecutive cases of illnesses in children during the dentition period. They included the following (1) Seventeen cases of pyelitis. The onset was usually acute, with high fever; treatment with sulphadiazine or other sulphonamide derivative in daily doses of 1 grain per pound body weight for three or four days was usually successful. Some children responded only to a second course of the drug or to calcium mandelate treatment. Intractable cases proved to be due to congenital malformations. (2) Nine cases of coeliac disease. Once the condition is fully developed the pale fatty stools can hardly be missed. The treatment is a high protein, low fat, diet with vitamin B and injections of liver extract. (3) Nine cases of nasopharyngitis and otitis media. Some children have little or no nasal discharge and since they cannot state the site of their pain the diagnosis may be missed. Adequate examination reveals the trouble. The treatment advised is administration of sulphadiazine. Constant watch must be kept on the ears, and paracentesis performed if necessary. (4) Eight cases of meningitis, two meningococcal, the rest tuberculous. The onset in the meningococcal cases was acute, with fever and vomiting; in the tuberculous cases it was insidious, with vague symptoms attributed in most of the cases to teething. Lumbar puncture clinches the diagnosis. In meningococcal meningitis sulphapyridine is indicated. (5) Six cases of stomatitis and gingivitis. Smears often show Vincent's spirochaete (*Borrelia vincenti*) and the fusiform bacillus. Gentian violet applied locally and vitamin C given internally will rapidly clear up the mouth. (6) Six cases of pink disease. Treatment consists in giving vitamins and artificial sunlight. (7) Two cases of milary tuberculosis; the condition here is hopeless. Symptoms sometimes associated with dentition are sleeplessness, loss of appetite, diarrhoea or vomiting and failure to thrive, and rashes. Organic disease having been excluded, treatment is given as common sense suggests.

Paterson, D. (1943) *Practitioner*, **150**, 225.

DERMATITIS DUE TO INJURY AND POISONING INCLUDING FEIGNED FRUPTIONS

See also B.E.M.P., Vol. III, p. 609; and Cumulative Supplement, Key No. 290.

Externally applied agencies, direct exposure

Toxic dermatitis

Contact dermatitis of the feet.—J. F. Burgess comments on the increasing incidence of dermatitis of the feet due to sensitization to various contacts, and the importance of differential diagnosis from various infective conditions. The clinical picture often simulates, in particular, an epidermophytosis, but the latter can be excluded by microscopical examination which demonstrates the absence of fungus. The diagnosis is made from the history of contact with new shoes or stockings, and the use of patch tests for sensitivity to the suspected material. Five cases are recorded; in one the patient was found to be sensitive to various kinds of shoe leather, and others were sensitive to fabrics used for insoles and linings.

Smoke dermatitis.—J. V. Landor, who reports an outbreak, finds in the literature only two references to dermatitis caused by smoke. His patients, thirteen in number and including men, women and children, were sent by the manager of a local brickworks to the General Hospital, Singapore, with a severe dermatitis affecting chiefly the exposed parts of the body. The lesions were very irritable, mostly vesicular and in some cases pustular. Examination for scabies gave negative results. All the cases had occurred in one row of coolies' dwellings. A Malay stated that firewood from the 'binjai' or wild mango tree had been used in the kitchen

of the affected coolie lines, and that the smoke of the wood was known by the Malays to be noxious. A sample was obtained and three preparations were made from it. A volunteer who submitted to a patch test of a steam distillate developed vesicular dermatitis within thirty-six hours, and a similar eruption was produced in guinea-pigs by applying compresses of the distillate to the shaved abdomen. All the patients responded to treatment with simple lotions when the use of binjai firewood was stopped.

Burgess, J. F. (1942) *Canad. med. Ass. J.*, **47**, 27.

Landor, J. V. (1943) *Brit. J. Derm.*, **55**, 17.

DERMATOSES, PYOGENIC

Treatment

Sulphonamide ointments

Optimum strength of ointments.—Sulphonamides in the form of ointments have been used by J. L. Miller for treating 112 patients with various skin diseases. The total number of colonies appearing in cultures made from the lesions was found to furnish a good index of the clinical condition. The diseases which were treated were classified as follows. (1) Primary infections of the skin, seventy-two patients; (2) secondary pyogenic infections complicating other conditions, forty patients. The drugs used were sulphanilamide, sulphathiazole, sodium sulphathiazole and sulphadiazine, in strengths of from 5 to 50 per cent. In patients with primary superficial pyogenic infection cure was obtained more quickly than by other methods of treatment. Thus of forty-five patients with impetigo contagiosa, all except one were cured in an average of six days. In syphilis and in other more deeply-seated infections the results were unsatisfactory. Secondary bacterial infections responded satisfactorily but the primary disease was unaffected. Severe reactions with a generalized eruption were observed in three patients, all of whom were being treated by 50 per cent sulphathiazole ointment, and two others had similar but milder reactions with a 10 per cent sulphathiazole preparation. With all the sulphonamide compounds a 5 per cent ointment was found to be just as effective as were preparations with higher concentrations. Sulphadiazine appeared to be less effective than sulphanilamide or sulphathiazole.

Miller, J. L. (1942) *Arch. Derm. Syph.*, N.Y., **46**, 379.

DIABETES MELLITUS

See also B.E.M.P., Vol. III, p. 644; and Cumulative Supplement, Key No. 296.

Diabetes mellitus

Pathogenesis

Effect of anterior pituitary substances. B. A. Houssay summarizes the advances which have been made in the last twenty-five years in our knowledge of the role of the hypophysis in carbohydrate metabolism. The chief facts which have emerged from much experimental and clinical work are as follows. Hypersensitivity to insulin of hypophysectomized animals is due to the loss of the anterior lobe. Increased sensitivity to insulin follows extirpation of the anterior lobe alone, and can be corrected by administration of anterior lobe substance. This anti-insulin effect is known as the glycotropic activity of the pituitary gland. In Simmonds's disease hypersensitivity to insulin has repeatedly been observed, and in acromegalic diabetes larger doses than usual of insulin are required, that is sensitivity is diminished. Hypophysectomized animals fall easily into hypoglycaemia and lose glycogen from the liver. Spontaneous hypoglycaemic crises may occur, they are associated with convulsions and may be fatal. A rapid fall occurs in hepatic and muscle glycogen during fasting, and can be prevented by giving anterior lobe extract. Remarkable amelioration in cases of experimental pancreatic diabetes occurs after total hypophysectomy or extirpation of the anterior lobe alone: life is prolonged, infections are less frequent, hyperglycaemia and glycosuria are less pronounced or absent; ketonaemia and ketonuria are slight. Subcutaneous implantation of anterior lobe re-establishes the diabetic condition. Phloridzin diabetes in dogs is similarly modified. The diabetogenic principle of the anterior lobe is sensitive to heat; the gland must be kept on ice after removal. Injection into normal mammals produces all the manifestations of diabetes. It acts through the liver and in hypophysectomized and pancreatectomized animals is suppressed by hepatectomy. Reasons put forward to account for its action include the increased production of sugar from endogenous protein, the depression of glucose oxidation and the stimulation of the liver to overproduction of glucose. The effect of anterior lobe upon ketone bodies is apparently dependent upon the liver, which must be functionally active for hyperketonaemia to occur.

Treatment

A new scheme of diet.—A new diabetic diet has been devised by A. C. Crooke and Ella Scott. The aim is to keep the total daily calorie value constant while allowing a free choice of foods. Each meal is arranged in terms of a given number of units, each equivalent to 50 calories. The patient is given a sample diet of 2,000 calories; units can be added or deleted as may be desired. He is also given a list of nearly 100 foods arranged in alphabetical order, showing the weight in ounces or fractions of ounces which is equivalent to 50 calories. The diet has been tried for a year on 528 diabetics classified as follows. (1) Requiring insulin: severe 107, mild 239, old 131. (2) Not requiring insulin: 51. The general level of health has been as good on

the new diet as on the old. No increase has been noted in the incidence of diabetic coma or of hypoglycaemic reactions; some of the most unstable of the patients have been more stable on the new diet. Of 192 patients requiring insulin who were observed for three months on the old and three months on the new diet, the body weight increased in eighty-six, diminished in thirty and was unchanged in seventy-six; insulin requirement increased in eighty-five, diminished in forty-six and was unchanged in sixty-one; glycosuria increased in twenty-two, diminished in fifty-three and was unchanged in 117. The blood sugar curves in eight in-patients were of the same order when the diet was a mixed one, was almost completely carbohydrate, or was mainly protein and fat. It is claimed that the new diet is more simple to use than are the old standard diets, that it allows the patient to adapt himself to war-time shortages of any particular food and that it is cheaper than diets containing more protein and fat.

Insulin resistance.—W. I. Glass, C. L. Spingarn and H. Pollack report the case of a Jewess, aged sixty, with glycosuria since 1930, and a history of pneumonia and diabetic ketotic acidosis in 1937. In January, 1940 the insulin requirement increased so that more than 85,000 units of insulin were given in observation over a period of five and a half months. During episodes of ketotic acidosis it was necessary to give 2,360, 2,500 and 2,795 units of insulin in the twenty-four hours. Later, treatment included X-ray exposures over the pituitary gland and the administration of lipocaine. After improvement a bowel infection with the Flexner dysentery bacillus occurred and increased the ketosis. Independently of this the liver was enlarged but not tender, and slight jaundice was noticed. The excessive insulin need subsided six months after its onset, and the patient was left with mild diabetes mellitus for six months. Cases of such an insulin-refractory state are infrequent, they have been divided into (1) those associated with some recognizable complication such as diabetic ketosis, an infection, an endocrine disorder, hepatic disease or other intercurrent illness, and (2) a smaller group of cases with a very high insulin-refractory state but without the aetiological factor mentioned in group (1). The authors' case belonged to group (2).

Single doses of different types.—A. R. Colwell, J. L. Izzo and W. A. Stryker have compared the effects in diabetes of single doses of insulin, protamine zinc insulin and mixtures of the two. Three patients were selected, two of them women, and all in a normal state of nutrition and free from acute complications. They were placed on a standard daily diet given in six four-hourly meals of similar composition. The urinary and blood sugar values were allowed to become constant before any insulin was given. Normal diurnal variations were observed, the levels tending to fall during the day and rise during the night. The curve was reversed in one patient kept up at night and allowed to sleep during the day, showing that activity is the factor responsible. In some cases the two insulins were mixed in the syringe, in others the mixture was allowed to stand at room or ice-box temperature before injection. No loss of potency was observed as the result of keeping mixtures for forty-seven days at room temperature. It was found possible to prepare mixtures showing any desired intermediate action between that of soluble and that of protamine zinc insulin, provided that they contained at least as much soluble as protamine zinc insulin. The peak effect is reached at from eight to sixteen hours, in contrast to four hours with soluble and twenty-four hours or later with protamine zinc insulin; waning of the effect begins at twenty-four hours. Thus if daily morning injections are given, the peak effect would fall in the late afternoon, and the waning would come during the early morning hours when the tendency to hypoglycaemia is greatest, both of which features appear desirable from the clinical point of view. These observations were confirmed in twelve diabetics treated for periods up to six months with mixtures containing 60 to 70 per cent of soluble insulin in single daily doses. The reason for the greater efficacy of mixtures than of soluble and protamine zinc insulin given in separate doses appears to be the formation of a chemically or physically modified insulin as the result of mixing the two kinds. The chief difficulty was found to be a tendency to hypoglycaemia in the late afternoon.

Diabetic coma

Treatment

Essentials of successful treatment.—E. P. Joslin, H. F. Root, Priscilla White and A. Marble, who have treated 525 cases of diabetic coma, the last sixty-two without a death, believe that almost every patient can be saved by proper treatment. They emphasize the fact that coma is a state of acute insulin deficiency which can be remedied only by giving adequate amounts of insulin, regardless of the number of units which this may mean. The commonest cause is laxity in treatment, consisting in either dietary indiscretions or neglect to take enough insulin or both; the next most common precipitating factor is infection. Death usually results from the interaction of various factors, of which age, duration of unconsciousness, degree of acidosis and the level of blood sugar, plasma carbon dioxide and blood non-protein nitrogen are the chief. In some cases death is due to a complicating infection, for which nowadays chemotherapy may offer a better chance of cure. Treatment should be carried out in hospital. The patient is warmed in bed while a sample of venous blood is taken for the determination of the blood sugar, plasma carbon dioxide, non-protein nitrogen and chloride content. The urine is also examined. Insulin administration must be begun at once and adequate doses given. The first dose is from 20 to 100 units (average 50 units) of ordinary insulin given subcutaneously, and if the patient is unconscious an equal amount may be given intravenously. A second dose of the same amount is given half an hour later, and in most cases at least two

other similar doses at half-hourly intervals are required. After two to three hours another sample of blood is examined. If the blood sugar and carbon dioxide show little or no return toward the normal, larger doses, for example 100 units at half-hourly or hourly intervals, should be given. If the return toward normal is satisfactory the doses may be reduced. Urine specimens are examined quantitatively for sugar every hour at first, later every two, three or four hours. Supply of fluid and chlorides is second only in importance to adequate doses of insulin; 1,000 to 1,500 cubic centimetres should be given intravenously, subcutaneously or by both methods, immediately after admission to hospital, and repeated once or twice within the first six hours. The addition of glucose is not advised. If circulatory collapse is present, continuous infusion of saline is started. As soon as the patient can drink he is made to do so; 4 to 5 litres of fluid at least should be given in the first twenty-four hours. Gastric lavage should be carried out as soon as possible and an enema given if abdominal distension is present. Feeding should be begun in from four to six hours; alkalis are never given.

Factors complicating the treatment of diabetes

Pregnancy, parturition and lactation

Main factors reviewed.—R. D. Lawrence and W. G. Oakley have studied the course of pregnancy and labour in fifty-four diabetic women. With the use of insulin many more diabetics conceive now than formerly, and while the maternal mortality has fallen dramatically as compared with that of pre-insulin days, the foetal and neonatal mortalities remain high. If a diabetic goes to term the child tends either to be over-sized, and is then often still-born, or to die without obvious cause within forty-eight hours of birth. The large size of the child is probably due to excessive supplies of sugar reaching the foetus from the maternal blood. Foetal hypoglycaemia may also account for part of the neonatal mortality, but evidence of this is unconvincing. The incidence of congenital anomalies in infants of diabetic mothers exceeds the normal. Maternal toxæmia is said to be unduly common in diabetics. In the present series only the first suggested cause was observed, and no relation could be established between the foetal weight and mortality. These large babies often showed signs of post-maturity. The maternal mortality rate was 2 per cent (one death from pulmonary embolism), the foetal, excluding therapeutic abortions, 33 per cent. Further analysis of the figures shows that when the mother was under regular supervision during pregnancy the foetal death rate was 28 per cent; when supervision was irregular or confined to the later weeks it was 50 per cent; and when supervision had not been exercised, it was 70 per cent. Special care is therefore needed to keep the mother's diet and metabolism balanced. The effect of pregnancy on diabetes is in most cases to increase insulin requirement; after delivery there is a reduction in the need of it. A subsequent increase in severity of the diabetes was not found to occur as the result of pregnancy. Severe ketosis is common during pregnancy and occurred in eighteen of the authors' cases. It responded readily to diet and insulin and appeared to be without influence on foetal mortality. The renal threshold is frequently lowered. A low renal threshold is one factor in the production of ketosis and increases the difficulty of managing the diabetes. Pregnancy may be encouraged in an intelligent, cooperative woman anxious to have a child. In others, pregnancy is discouraged, and should it occur therapeutic abortion with sterilization then or later is advised. A family history of diabetes mellitus on either side is a strong reason for avoidance or termination of pregnancy. During pregnancy close supervision is essential. Ketosis and hypoglycaemia should be avoided on the mother's, and hypoglycaemia on the baby's, account. The low renal threshold and the increased sugar tolerance during and after labour add to the risk of hypoglycaemia. It is wise to terminate a first pregnancy early, because Caesarean section or induction of labour at the thirty-sixth or thirty-eighth week offers a better chance of a living child than spontaneous delivery at term. Neonatal hypoglycaemia may occur, and the infant should receive glucose two-hourly for the first twenty-four hours. The secretion of milk is often deficient in diabetics and test feeding should be carried out as a routine.

EDITORIAL COMMENTARY—Twenty Years of Progress in Diabetes Mellitus

During the past twenty years there has been no single advance in the treatment of diabetes in any way comparable with Banting and Best's discovery of insulin, the most outstanding therapeutic contributions being the introduction of protamine insulin by Hagedorn in 1935, and its subsequent modification into protamine zinc insulin in the following year by Scott and Fisher. Our knowledge of carbohydrate metabolism, however, during the same period has increased greatly, and the important part played in it by the anterior lobe of the pituitary gland has been demonstrated in animals by the brilliant researches of Houssay, Evans, Young and others.

The production of permanent diabetes in dogs by repeated injections of pituitary extract first carried out by Young in 1937, and the demonstration by Young and Richardson (1938) of histological changes in the island cells of the pancreas of animals so treated similar to those found in human diabetes, constitute perhaps the most important experimental advance of recent times. Young's work has not only demonstrated conclusively the great significance of the pituitary gland in carbohydrate metabolism but has also provided a method of investigating, without pancreatectomy and its inevitable operative and digestive disturbances, the influence of factors such as species, age, sex and diet upon the production of experimental diabetes in animals. The pituitary extract used in these experiments appears to contain at least

three hormones which influence carbohydrate metabolism: the first or glycogenic renders the animal insensitive to the hypoglycaemic action of insulin, the second or diabetogenic produces the rise in blood sugar, and the third or pancreatrophic causes hypertrophy and hyperplasia of the cells of the islands of Langerhans.

The type of response obtained as a result of injecting the extract varies according to a number of factors of which age and species are of particular interest. F. G. Young (1941) found that puppies responded not by the production of hyperglycaemia and glycosuria but by a rapid increase in growth, and that not until they became incapable of further response in this direction did diabetes develop. This suggests a possible relation between the growth and so-called diabetogenic hormones, and is of interest when considered in connexion with the view held by Joslin, White and others that the majority of diabetic children are tall and over-developed for their age at the onset of the disease.

The response of various species of animals has been studied, and it has been found that, whereas the dog can be made permanently diabetic with comparative ease, the rat is highly resistant to the diabetogenic hormone; this is probably due to the fact that rats are more sensitive than dogs to the action of the pancreatrophic fraction of the extract, the existence of which was first suggested by the work of Anselmino, Herold and Hoffman (1933) on this animal. The importance of species variation must be remembered when the significance of these animal experiments is considered in relation to the problems of human diabetes.

If the past six years have not seen the entry of any great new weapons into the therapeutic armamentarium they have, nevertheless, given an opportunity to clinicians to increase their knowledge of the slow-acting insulins and of their skill and ingenuity in using them. It is now widely recognized that protamine zinc insulin by itself can be expected adequately to control only relatively mild diabetes, any attempt to control the hyperglycaemia which follows meals in severe cases being either unsuccessful or necessitating doses so large as to involve grave risk of serious nocturnal hypoglycaemia. In order to overcome this difficulty protamine zinc insulin has been combined with clear soluble insulin either in two separate injections or as a mixed dose, both insulins being introduced into the same syringe. Recently investigations have been made, the results of one of which are summarized above, into the resulting composition and consequent action of such mixtures, and it has been shown that a considerable proportion of the soluble insulin is converted into the slow-acting compound by the excess of protamine present in the latter.

New insulin compounds such as globin insulin (L. Reiner, D. S. Searle and E. H. Lang, 1939) and histone insulin (C. C. Bailey and A. Marble, 1942) have undergone therapeutic trials in hopes that a single preparation may be found which will possess both a strong rapid and weaker prolonged action, but it is as yet too early to pass judgment upon them.

The search for a preparation of insulin which will retain its hypoglycaemic action when given by mouth continues and, although the problems of overcoming inactivation by digestive enzymes and promoting gastro-intestinal absorption have not yet been solved, the recent work by P. J. Hanzlik and W. C. Cutting (1941) and W. C. Cutting and G. B. Robson (1941) has raised the hope that a satisfactory solution may yet be found. These workers have shown that a definite, but transient, hypoglycaemia can be produced by the oral administration of a mixture containing insulin and quinine, but the fact that even moderately severe diabetes are not controlled by a daily dose of 1,500 units of insulin given in this way serves to emphasize the difficulties yet to be overcome.—WILFRID OAKLEY.

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DIARRHOEA ASSOCIATED WITH FLAGELLATE INFECTION

See also B.E.M.P., Vol. IV, p. 12; and Cumulative Supplement, Key No. 306.

Giardia intestinalis

Clinical picture

Epidemic features and treatment.—An outbreak of enteritis associated with *Giardia lamblia* infestation is reported by G. Ormiston, Joan Taylor and G. S. Wilson. It occurred in a country house used partly as a family residence, partly as a nursery home for evacuees. The domestic arrangements were separate but there was free communication between the two

communities. In all, eighty-six per cent of the people became infested and cases continued to occur from July, 1940 to May, 1941 when treatment brought the outbreak to an end. The symptoms included diarrhoea and vomiting, and in the adult patients there were abdominal pain, giddiness, headache, backache and fever. All the adult patients recovered but two of the infants died. Microscopical examination of the stools from several of the patients showed *Giardia lamblia*, and led to an examination of the stools of the remainder of the inmates. Of the entire household (including twenty-nine children and twenty-two adults) 45 per cent of the children and 27 per cent of the adults were found to be harbouring the parasite. A large proportion of the carriers had either loose stools at the time of the examination or a history of diarrhoea, a fact which suggests, although it does not prove, a connexion between the *Giardia* infestation and the enteritis. The outbreak was treated as follows. Six children heavily infested with *Giardia* were isolated in a cottage near by in charge of two nurses, one infested and one not infested. Quinacrine (mepacrine hydrochloride) was given in doses of 0.5 gramme (8 grains) daily to the children and 3 grammes (45 grains) daily to the infected nurse. After five days all stools were negative. To make certain of cure a second course of quinacrine was given, and at the end the stools again were all negative. Since the treatment had been successful and toxic symptoms had not appeared, it was applied to the other infested persons at the large house; two courses were given, and all stools were found to be negative after the second course. The nursery part of the house was disinfected after the first course. No serious toxic manifestations occurred; there were some cases of slight yellow coloration of the skin and urine. The stools of many of the inmates were re-examined at intervals up to February, 1942. Three fresh cases occurred and two of the children relapsed or became reinfested. The failure to stamp out the infestation may have been due to carriers among a few adults who refused to be examined or treated.

Steatorrhoea - A case of steatorrhoea associated with giardiasis, the second to be recorded in Ireland, is described by D. K. O'Donovan, J. McGrath and S. J. Boland. A boy aged nine and a quarter, was first seen in February, 1941 suffering from retardation of growth, from attacks of diarrhoea with pale, bulky stools and from vague abdominal pains, especially in the left iliac fossa; he had an enormous appetite, particularly for sugar. He was anaemic, small and undernourished. X-ray examination showed dilatation, segmentation and absence of normal pattern in the mucous membrane of the lower part of the small intestine and slight decalcification of the long bones. The stools were pale brown, and contained an excess of fat crystals; analysis showed that 45 per cent of the fat ingested was being excreted in the faeces. Parasites were found only after purgation with sodium sulphate, when the liquid stool contained the encysted form of *Giardia lamblia* in large numbers. After purgation the diarrhoea subsided, and three weeks later analysis of the stools yielded results within normal limits. Five subsequent attempts to find parasites after purgation were failures, and the boy was sent home six weeks after admission. Re-examined in February, 1942 he did not show any striking general improvement although the diarrhoea had not recurred. The appetite remained excessive. Atebrin (mepacrine hydrochloride) had been given for five days in January, 1942 without effect. In view of the permanent changes in the intestinal mucous membrane caused by the parasite, and of the absence of the latter from the stools except after purgation, the authors suggest that supposed idiopathic steatorrhoea sometimes results from unrecognized giardiasis in childhood.

O'Donovan, D. K., McGrath, J., and Boland, S. J. (1942) *Lancet*, 2, 4.

Oimiston, G., Taylor, Joan, and Wilson, G. S. (1942) *Brit. med. J.*, 2, 151.

DIARRHOEA IN INFANCY AND CHILDHOOD

See also B.F.M.P., Vol. IV, p. 21; and Cumulative Supplement, Key No. 308.

Pathology and bacteriology

Bacteriology

Sources of infection in epidemics among infants.—Four epidemics of infectious diarrhoea of the new-born have been studied by W. B. McClure. In hospital A two outbreaks occurred. Rectal swabs and faecal specimens taken from infants with diarrhoea showed a much higher incidence of haemolytic colon organisms than those from the unaffected infants: of twenty-four sick infants, twenty-one yielded a haemolytic colon organism, whereas of nineteen normal infants all gave negative results. The bathing table, after the infants had been changed on it, showed haemolytic colon organisms of the same strain as was found in six of the infants and in one of the nurses. Three of the seventeen nurses, one of whom was responsible for making up feeds, yielded other strains of the same organism. In hospital B haemolytic colon organisms were isolated from nine out of twenty-one infants. In hospital C faecal samples were not examined, but the evaporated milk made up for twenty-four hours, as well as the nipple jar, yielded an abundant growth of haemolytic colon organisms. In hospital D, in which five fatal cases occurred, both colon and paracolon haemolytic organisms were isolated from most of the sick and from some of the convalescent infants. Live cultures of the haemolytic organisms isolated from sick infants were fed to four cats and four kittens; in two of the cats diarrhoea developed. No symptoms occurred in a human volunteer who swallowed live cultures, or in mice and guinea-pigs to whom they were fed. Grown in an atmosphere containing 10 per cent of carbon dioxide, the organisms referred to produced toxins which caused illness and some-

times death when injected into cats. The degree of susceptibility shown by the cats varied, and some animals were non-susceptible. Immunity did not appear to develop after repeated injections in susceptible cats. Artificial feeding and the bathing and changing of the infants appeared to be the most potent causes of infection.

Treatment

Specific

Symptomatic and curative—Treatment of diarrhoea in infancy is considered by C. Harris under two heads, the treatment of (1) the effects, and (2) the cause. The constitutional effects of severe infantile diarrhoea include collapse, dehydration, ketosis, acidæmia, uræmia and protein loss, and they must be overcome if the child is to be kept alive long enough to allow the cause of the diarrhoea to be treated. The child must be kept warm and quiet and may need stimulants, of which nikethamide (0.5 cubic centimetre) is best, with lobeline ($\frac{1}{10}$ grain or 0.003 gramme) if the respiratory centre is failing. Loss of body fluid must be replaced and continuous intravenous infusion is the method of choice. The reservoir of the drip apparatus may be filled alternately with isotonic or hypertonic saline and with from 5 to 10 per cent glucose solution and, if ketosis is severe, 5 units of insulin should be given during the period of glucose administration. Cortin (extract of suprarenal cortex), 0.5 cubic centimetre, given subcutaneously every four to eight hours, assists rehydration. To combat acidæmia, a buffered solution such as Hartmann's may be used at intervals in the intravenous drip. Lost protein should be replaced by infusion of plasma, 10 cubic centimetres being given for each kilogram of body weight, as soon as dehydration has been corrected. If the child does not sleep, morphine ($\frac{1}{100}$ grain or 0.00015 gramme for each year of age) or chloral hydrate may be given. The skin of the buttocks requires careful attention. After the constitutional disturbance has been overcome, and in cases in which it is absent, the cause of the diarrhoea must be sought and treated. If the diarrhoea results from ingestion of some irritant a single dose of castor oil is administered, and water (or sugar and water) only is given by mouth for a day; bismuth or some similar drug may be required if the diarrhoea continues. If the condition is infective in origin and is accompanied by fever, the initial purge is omitted. Apple-pulp is useful for treatment after the starvation period. If organisms of dysentery are isolated from the stools, administration of sulphaguanidine (0.15 gramme per kilogram of body weight daily) gives good results.

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DIETETIC DEFICIENCY DISEASES

See also B.E.M.P., Vol. IV, p. 51.

Prevalence of deficiencies

Deficiencies in other parts of the world

Incidence in California—A survey has been made by M. A. Krupp in California of about 400 consecutive hospital admissions, in order to estimate the nutritional state of the population group concerned during the winter of 1940-41. The patients mostly belonged to the low and middle income classes; they were of all ages and as a rule had some chronic medical disorder. The difficulty of obtaining a satisfactory dietary history and of determining what constitutes vitamin deficiency is emphasized, and the figures given below must be taken as approximate. It was estimated that the diet was inadequate in 22.9 per cent of the whole group, and that the percentage was much higher in the lower income than in the higher income class (46 per cent as compared with 20.7 per cent). Of the patients who took inadequate diets 11.4 per cent showed signs of vitamin deficiency. No case of clinical scurvy, beri-beri, pellagra or keratomalacia was seen. Four cases of oedema appeared to be due, in part at least, to poor diet. Twelve patients showed minor signs of vitamin deficiency, usually of vitamin B. In the group taking an adequate diet only 0.67 per cent showed evidence of lack of vitamins, which indicates that serious organic disease *per se* is not usually a cause of deficiency disease. In the entire group the number of patients showing clinical evidence of some vitamin deficiency was 3.1 per cent.

Deficiency of the vitamin B complex

Diseases due to vitamin B deficiency

Testing with thiamine.—R. D. Williams, H. L. Mason, Marschelle H. Power and R. M. Wilder continue the investigations at the Mayo Clinic. The first research on isolated thiamine deficiency was made in 1939 on four young women having a basal diet which provided 0.15 milligram of thiamine per day, and which was planned by R. D. Williams, H. L. Mason and B. F. Smith. A further research was carried out in 1940 by Williams, Mason, Wilder and Smith. The periods of restricted thiamine varied from a few weeks to several months; the patients—volunteers—were chosen from the inmates of a large psychotic hospital, who were capable of consenting or whose relatives could do so. Among the human volunteers only those who were deprived of thiamine showed multiple neuritis. Evidence of signs and symptoms of deprivation of thiamine appear after weeks or months in the form of dysfunction of the sensory nervous pathways, but the earliest evidence may be low levels of thiamine excretion in the urine. Almost simultaneously with a significant fall of excretion of the test dose of

thiamine the values for pyruvic acid in the blood after the administration of dextrose become raised and the subjects become listless, progressing to apathy, anorexia, fatigue and nausea. In the earlier observations on the induced thiamine deficiency the experiment now appears to have been too drastic and to have made its abandonment necessary before the nervous symptoms appeared. Multiple neuritis was a manifestation of late rather than early, severe rather than mild, deficiency of thiamine, representing an anatomical defect which was only slowly reversible even when thiamine hydrochloride was given intensively.

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— Power, Marschelle H., and Wilder, R. M. (1943) *Arch. intern. Med.*, **71**, 38.

DIPHTHERIA

See also B.E.M.P., Vol. IV, p. 72; and Cumulative Supplement, Key No. 324.

Complications

Circulatory failure

Electrocardiographic observations —C. Neubauer advocates electrocardiography in all but the mildest cases of diphtheria. He gives an account of 100 patients with cardiac disorders, dividing them into three groups. (1) Patients with general myocardial damage. The chief clinical signs are listlessness, pallor and increased or decreased pulse rate. Albuminuria may be present and, when pronounced in the early stages, is of bad omen. Electrocardiograms often show alterations of the T wave, in the S-T interval or in both. Dislocation of the S-T stretch is an important sign, but variations due to meteorism or to digitalis administration must be borne in mind and they are a normal finding in lead III. The electrocardiogram returns to normal in from three to thirteen weeks, according to the severity of the case, and a child with a myocardial lesion should not be discharged from hospital until a normal tracing is obtained. (2) Patients with abnormalities of rhythm. Sinus tachycardia, often seen in the febrile period, is unimportant. Sinus bradycardia may or may not be due to myocardial damage. The only importance of sinus arrhythmia lies in the possibility of its being considered pathological and made a reason for unnecessary restriction of activity. Extrasystoles are not of serious import. (3) Patients showing interference with conductivity. Auriculo-ventricular block, partial or complete, is always serious. Electrocardiography is required for diagnosis. Partial block was found in seventeen, complete block in five of the patients. Bundle-branch block, partial or complete, can be diagnosed only by electrocardiography. Partial block occurred in nineteen, complete block in four children. Auricular fibrillation may occur in severely damaged hearts, or as a transient phenomenon in undamaged hearts. Transient fibrillation was noted in two patients in the series.

Neubauer, C. (1942) *Brit. med. J.*, **2**, 91.

DISLOCATIONS, FRACTURES, FRACTURE-DISLOCATIONS, AND ASSOCIATED INJURIES

See also B.E.M.P., Vol. IV, p. 113; and Cumulative Supplement, Key Nos. 326-353.

Treatment

Union

Delayed union — R. Watson-Jones and W. D. Coltart examine the recent allegations (1) that fractures of the shaft of the tibia and femur unite more slowly than in former years, and (2) that modern methods of treatment are to blame. They point out that the times of union given in early text-books were based on clinical and not on radiological examination, and quote contemporary evidence that yielding, malunion and nonunion quite often occurred after the patient was out of the surgeon's hands. Nowadays protection is continued until consolidation is radiologically complete, malunion and nonunion have practically disappeared. A fixed time for union cannot be laid down: every fracture unites if it is immobilized long enough. Of 804 cases reviewed by the authors, despite a high proportion of comminuted and infected fractures, none failed to unite. The causes of slow union must be local, since a general cause such as dietary deficiencies would operate equally in all fractures, not only in those of the tibia and femur. Investigation of the present series of cases shows three local factors of outstanding importance: (1) interrupted immobilization; (2) infection of the fracture; (3) distraction of the fragments. In all cases two or more of the above factors were operative. Other causes of delay are impaired blood supply, interposition of an avascular fragment and angulation, especially when combined with early weight-bearing which distracts the fragments on the open side of the angle. Of early weight-bearing 'the gain is doubtful, the danger is real'. Interruption of immobilization may be deliberate, when primary reduction fails, or accidental, during the changing of a plaster. Serious interruption results from the practice of gradual reduction by weight-traction. Reduction should be immediate, never more than twelve hours after the injury, and performed under anaesthesia, with or without weights. Once interruption is stopped union proceeds normally. Distraction acts differently; callus formation is delayed and the time taken to unite after distraction ceases is greatly prolonged. Traction, even without distraction, delays union in the tibia; internal fixation does not do so. Infection in open frac-

tures slows the rate of union but every infected fracture will unite without shortening if immobilization is complete and prolonged. Delay can be reduced by early excision of the wound, early sequestrectomy and early skin-grafting.

Compound fractures

Experimental results of chemotherapy.—Experimental and clinical studies in the treatment of open fractures by local application of sulphanilamide are reported by N. K. Jensen and M. C. Nelson. For the experimental work guinea-pigs were chosen. A standard open fracture was produced under ether anaesthesia by incising the pectoral muscles and breaking a rib; if the pleura was accidentally opened the animal was discarded. The wound was inoculated with known numbers of organisms and in most cases was closed with silk, a few wounds only being left open. In the first series of experiments cultures of *Staphylococcus aureus* were used to contaminate the wound. The animals were divided into three groups. In one group sulphanilamide powder was introduced into the wound prior to closure, in the second group sulphanilamide was given systemically; a third (control) group did not receive any sulphanilamide. The results were as follows. In group (1) with 20 per cent of infected wounds, there were not any deaths. In group (2) with an 80 per cent infection rate, there was 20 per cent mortality. In group (3) with a 71 per cent infection rate, there were not any deaths. The efficacy of local sulphanilamide was tested in relation to the numbers of organisms introduced into the wound, and it was found that, with a high degree of contamination, sepsis was not prevented but that the incidence of fatal sepsis was reduced. In the presence of foreign bodies or dead tissues, the efficacy of the drug is greatly diminished. In a second series of experiments the wounds were inoculated with a mixture of cultures of staphylococcus, streptococcus and *Clostridium welchii*. Two groups of animals were used; those in the first were treated by the local application of sulphanilamide, whereas those in the second were not given any. The results were as follows. Group (1) no gas gangrene, no deaths; group (2), gas gangrene, 100 per cent, mortality, 80 per cent. The antibacterial action of sulphanilamide appears to be greater when the wound is kept at a temperature of 37 °C., or above it, for the first twenty-four to thirty-six hours. The clinical material comprised 212 cases of compound fracture, which were mostly due to road accidents; all the cases were treated by local implantation of sulphanilamide after scrupulous debridement, by closure of the wound whenever it was considered safe, and by closed plaster. The results showed that local sulphanilamide treatment reduced the incidence of infection in open fractures from approximately 27 per cent to 3.3 per cent, and reduced the average stay in hospital from 96.3 to 30 days. Two of the 212 patients (0.9 per cent) developed gas gangrene, as compared with 7.3 per cent of a control series in which the patients were treated without sulphanilamide.

Regional

Fractures of shafts of tibia and fibula

Fatigue fracture of the tibia—J. B. Hartley describes fourteen cases of 'fatigue fracture' of the tibia. The lesion consists of an incomplete fracture from two and a half to three inches below the knee joint, and is often bilateral (in three cases in the author's series). True fracture may occur at the site of the lesion if the latter is not recognized and treated. Fatigue fracture is most common in adolescence; patients complain of pain at the upper end of the tibia or in the calf, the pain disappearing on resting. A history of injury is rarely obtained. Tenderness was present in three of the cases and slight swelling in five, the average age was thirteen years, the oldest patient being twenty. The length of the history was between ten and twenty-one days, and in the radiograph callus was invariably present by the time the patient came under observation. Treatment consists in absolute rest with the limb in plaster for several weeks, investigation for causes of abnormal stress and strain, and improvement of the patient's nutrition, with special regard to calcium intake. If a zone of osteoporosis develops rapidly it may be advisable to explore the bone, but, in three cases of the author's in which exploration was made, pus was not found.

Foot

Fractures of the os calcis treated by triple arthrodesis.—The extremely bad results ordinarily obtained in crush fractures of the os calcis leads A. S. B. Bankart to advocate immediate triple arthrodesis as a routine treatment. Two patients whom he has so far treated by the above method have active painless feet. A slight modification of the usual technique overcomes the difficulty of dislocating the foot inwards at the subastragaloid joint without completely disrupting the bone. A short longitudinal incision is made over the scaphoid bone; this is excised and the cartilage is removed from the head of the astragalus and the bases of the cuneiform bones. The incision is then closed, the usual incision is made on the outer side of the foot and the calcaneocuboid joint is excised. The subastragaloid joint is now opened and dislocation of the os calcis is easy. The articular surfaces are removed piecemeal and the fragments of the os calcis are manipulated in order to restore the prominence of the heel. The foot is then displaced backwards and the operation is completed. The foot is kept in plaster for four months, during which time weight-bearing is not allowed.

Bankart, A. S. B. (1942) *Lancet*, 2, 175.

Hartley, J. B. (1942) *Brit. J. Surg.*, 30, 9.

Jensen, N. K., and Nelson, M. C. (1942) *Surg. Gynec. Obstet.*, 75, 34.

Watson-Jones, R., and Coltart, W. D. (1943) *Brit. J. Surg.*, 30, 260.

DISSEMINATED SCLEROSIS

See also B.E.M.P., Vol. IV, p. 187; and Cumulative Supplement, Key No. 354.

Pathogenesis*Theories of pathogenesis*

Blood coagulation.—Studies of the blood coagulation time in disseminated sclerosis and in other diseases of the brain stem and cord have been undertaken by B. Simon. Twenty patients were divided into two groups, consisting of ten patients with disseminated sclerosis and ten with miscellaneous lesions. With the method of estimation employed, the clotting time in normal subjects ranged from twenty-five to forty-five minutes; a deviation of less than ten minutes was not considered to be significant. Two experiments were conducted on each patient; in one fever was induced by intravenous injection of typhoid vaccine, in the other the physiological effects of emotional excitement were counterfeited by subcutaneous injection of adrenaline. Both groups reacted to each experiment with a reduction of coagulation time, but this was much more pronounced and enduring in the patients with disseminated sclerosis than in patients with other diseases. The theory is postulated that a congenital or acquired disorder of clotting, consisting in abnormal sensitiveness to the exogenous or endogenous stimuli which tend to reduce coagulation time, produces diffuse intravascular clotting and that this is the underlying cause of disseminated sclerosis.

Clinical picture*General review*

T. J. Putnam reviews the history of multiple sclerosis during the nineteenth century, from the time of Sir Robert Carswell, professor of Pathology in London University, who gave an illustration in 1838 of the lesion, of J. Cruveilhier who gave a more complete account, and of J. M. Charcot whose well known description of '*sclérose en plaques disséminée*' was based on observation of a servant in his own house and on her necropsy at the Salpêtrière. The further developments show that the disease is by no means rare, especially in its milder forms. Owing to variations in standards of diagnosis it is difficult to estimate its incidence, its diagnosis is stated to be more often missed than erroneously made. There is a pronounced difference in its local incidence; it is common in the Baltic Countries, Scotland, the North Atlantic seaboard and the Great Lakes region. It is rare in the Mediterranean and in South America and almost unknown in China, Turkey, India and Japan. It is characterized pathologically by glial scars scattered throughout the nervous system. Putnam agrees with O. Marburg and those who believe that the disorders characterized by scars interspersed with acute lesions represent merely the chronic relapsing form of the acute demyelinating diseases, which include post-infective and disseminated encephalomyelitis, Schilder's disease, diffuse sclerosis, neuromyelitis optica, acute transverse myelitis, and 'idiopathic' optic and retrobulbar neuritis. The histopathology of these disorders is fundamentally uniform. The acute disorders comprise the great majority of the cases of 'encephalitis' seen in practice. There is not one single syndrome that can be considered typical of multiple sclerosis and the demyelinating diseases. A large number of symptoms may occur; weakness or numbness of one or more extremities, tremor, ataxia, nystagmus, speech defects, emotional susceptibility, retrobulbar neuritis or papillitis with central scotoma, diplopia, vesical disturbance. The course of symptoms is often characteristic; they sometimes come on within a few minutes or overnight; a patient may watch a scotoma develop or be thrown down by an attack of hemiplegia. Some neurologists believe that the course of the demyelinating disease is more stormy in children, more gradual in middle life; an onset after forty is unusual. A study of the lesions show that it is impossible for a large number of axis cylinders to be destroyed in the acute phase.

Putnam, T. J. (1943) *Bull. N.Y. Acad. Med.*, **19**, 301.

Simon, B. (1942) *Arch. Neurol. Psychiat.*, Chicago, **48**, 509.

DIVERTICULOSIS AND DIVERTICULITIS

See also B.E.M.P., Vol. IV, p. 207; and Cumulative Supplement, Key No. 355.

Stages*Diverticulitis*

Proctoscopy in the diagnosis—The value of proctoscopy in the diagnosis of acquired diverticula of the colon is the theme of a paper presented by R. J. Jackman and L. A. Buie to the Section on Gastro-Enterology and Proctology of the American Medical Association. Although the diagnosis depends primarily on the X-rays, proctoscopy can be of assistance in differentiating between diverticulitis and carcinoma; and examination of the bowel per anum or through a colostomy may be useful when an emergency operation has been performed to relieve obstruction the nature of which cannot be ascertained at the time because of the general condition of the patient. The five proctoscopic signs pointing to diverticulitis or diverticulosis are as follows. (1) Limited mobility of a segment of bowel which is normally freely movable. (2) Angulation of the bowel. (3) Reduced lumen and adherent mucosal folds. (4) Sigmoidal sacculcation. This sign consists in the appearance of shallow pouches extending partly or wholly round the wall of the bowel. (5) Visualization of the mouth of the diverticulum. This is more often possible than is generally supposed. It is seldom obtained in cases in which inflammation is present. The value of these signs was corroborated by a study of

250 cases, in eight of which an X-ray examination was not made since in all of them proctoscopy enabled the diverticula to be seen. Of the remaining 242 cases, the results of endoscopy were negative in eighty-two. In 160 cases (66 per cent) one or more of the above-mentioned signs were present. In three cases sacculations were noticed on proctoscopy but radiological evidence of diverticulosis was not obtained; at periods varying from one to six years later further X-rays revealed diverticula. To ascertain the value of endoscopy after colostomy fifty patients were studied. In all, colostomy had been performed for obstruction and a diagnosis had not been made. In thirty-seven (74 per cent) of these patients the evidence obtained was sufficient to enable a diagnosis to be made. In many cases the examination had to be repeated several times because individual loops were at first inaccessible owing to inflammation and fixation. In the remaining cases diagnosis was made only by the pathologist.

Jackman, R. J., and Buie, L. A. (1943) *J. Amer. med. Ass.*, **121**, 1144.

DRUG ADDICTION

See also B.E.M.P., Vol. IV, p. 246, and Cumulative Supplement, Key No. 359.

Clinical picture

Abstinence symptoms

Visual hallucinations in paraldehyde addiction.—M. Heiman reviews the literature relating to visual hallucinations in paraldehyde addiction, and concludes that they are of a specific type. They occur as a rule during the withdrawal period, and are usually very intense and associated with hallucinations of other senses. The author reports the case of a salesman, aged forty-six, who had been taking from 15 to 30 grammes of paraldehyde daily for five years. He had become an addict during a period of treatment (the second) for morphine addiction. In the last four years previous to examination he has experienced at intervals a hallucination which consists of a symmetrical network into which he seems to be about to run, and which appears to be three-dimensional in its extension. The network is green at the centre, yellow towards the periphery; as he advances towards it the centre appears red. It fills the whole visual field and is in constant kaleidoscopic movement. The interstices are filled with leaves like ferns, so thick that he cannot see through them. The 'forest' appears on walking from a light room into the dark; the further he proceeds into the darkened room the more distinct becomes the foliage. If the light becomes sufficiently dim he becomes disorientated and stops, and immediately the meshwork becomes convex, moving towards him, and the centre becomes more distinct, the periphery more hazy. Just as he approaches the convexity the structure becomes plane again. The patient experiences a sensation of 'frightfulness' and tries to avoid the phenomenon by looking to right or left, but wherever he looks it meets his eyes. When he reaches the bathroom and turns on the light it becomes flattened out on the walls 'like wall-paper', and then disappears. The author connects the hallucination with a former experience, when during a morphine-withdrawal period the patient, crossing the hall, saw a plant in a pot standing on a small table. The plant consisted almost entirely of stalks, and suddenly appeared hugely magnified, giving the impression of a forest standing in his way. The phenomenon resembles mezzanine hallucinations. Its illusionary movement may be explained as being due to a disturbance of vestibular function.

Heiman, M. (1942) *J. nerv. ment. Dis.*, **96**, 251.

DRUG ERUPTIONS

See also B.E.M.P., Vol. IV, p. 261; and Cumulative Supplement, Key No. 360.

Types of drug eruptions

Granuloma

Magnesium silicate granuloma—T. L. Ramsey records four more examples of this foreign-body granuloma which shows fibroblastic proliferation. Its development is due to the irritation set up by crystals of magnesium silicate in talcum powder. The complication may be serious, for example in intestinal granulomas causing obstruction. The author lays stress on the danger of the use of the powder in surgical practice. Care should be taken not to regard every slide preparation showing the crystals as evidence of the granuloma; the points of diagnostic significance are the presence of the crystals in the lesions and especially in the giant cells. W. M. German has shown that the histological features are those of lupoid sarcoid.

German, W. M. (1940) *Amer. J. clin. Path.*, **10**, 245.

Ramsey, T. L. (1942) *Amer. J. clin. Path.*, **12**, 553.

DWARFISM AND INFANTILISM

See also B.E.M.P., Vol. IV, p. 277.

Clinical picture

Dwarfism combined with infantilism

Ovarian infantilism.—F. Albright, Patricia H. Smith and R. Fraser describe eleven cases of a syndrome characterized by and probably due to lifelong ovarian insufficiency. The features of the syndrome are primary amenorrhoea, shortness of stature without actual dwarfism, infantile genitalia and mammae, scanty growth of axillary and pubic hair which becomes normal with oestrin therapy, good physical condition, slight retardation of bone age with

ultimate union of the epiphyses, a constantly increased urinary excretion of follicle-stimulating hormone and a somewhat diminished '17-ketosteroid' excretion, and a normal hypoglycaemic response to insulin tolerance tests. There is frequently co-existence of other congenital anomalies, especially coarctation of the aorta and webbing of the neck, and there is a tendency to diffuse osteoporosis and early senility. The differences between patients so affected and pituitary dwarfs are these: pituitary dwarfs are shorter, their bone ages are very much retarded and the epiphyses may never unite; they lack pubic or axillary hair, and oestrin therapy does not produce any additional growth, they tend to be weak and undernourished; the urine does not contain any follicle-stimulating hormone and practically no 17-ketosteroids, and the insulin tolerance test shows lack of hypoglycaemic response. The average height of the eleven subjects was four feet seven inches. Reasons are given for believing that the decreased rate of growth is due to secondary changes in the adrenal cortex rather than to the primary effect of oestrin deficiency. The low 17-ketosteroid excretion points to a disorder of cortical function, and the theory is advanced that oestrin deficiency leads to decreased production of luteinizing hormone by the anterior lobe of the pituitary gland and that this induces adrenal cortical hypofunction. The growth of the axillary and pubic hair is thought to be controlled by the adrenal cortex, and the fact that oestrin therapy increases such growth suggests a stimulating action of oestrin on the adrenal glands. Oestrin increases the rate of growth in subjects whose epiphyses are still ununited and stimulates development of the breasts.

Albright, F., Smith, Patricia H., and Fraser, R. (1942) *Amer. J. med. Sci.*, **204**, 625.

DYSENTERY, BACILLARY

See also B.E.M.P., Vol. IV, p. 317, and Cumulative Supplement, Key No. 364.

Clinical picture

Clinical types

Flexner dysentery in a hospital. —W. A. Caldwell and S. W. Hardwick describe an outbreak of Flexner dysentery in an infirmary. Starting in a female ward, it spread to other parts of the hospital in which, between December, 1940 and May, 1942, 357 cases of dysentery or of severe diarrhoea occurred. Two peak periods were noted, in the winter and in the early spring months; the occurrence of these was probably due to the fact that contact is closer in cold weather when the patients go out less. Not one case of proved dysentery occurred in a 'parole' or 'open' ward, in which the patients spend a large part of the day away from their quarters. Faecal specimens grown in Hynes's medium yielded a high percentage (about 70 per cent in the female cases) of Flexner positive results; rectal swabs gave a much lower percentage of positives. The symptoms on the whole were mild. Pyrexia was moderate, severe dehydration was rare and complications were uncommon. Most patients became symptomless in ten days but continued to pass organisms in the faeces for lengthy periods. The majority of patients were treated by sodium sulphate. Sulphapyridine and sulphaguanidine were given in some cases. Good results were obtained with the latter drug in early cases and the carrier stage appeared to be shortened.

Diagnosis

Laboratory diagnosis

Faecal and serological examinations. —P. H. Manson-Bahr, in the first of two lectures dealing with dysentery and diarrhoea in war-time, describes acute bacillary dysentery as the most important type in war-time and the main cause of the Gallipoli failure. The diagnosis is difficult because the organisms quickly vanish from the stools. They are seen abundantly in microscopic sections and may persist for years in retention cysts in the mucosa; with such lesions about 20 per cent of patients become carriers. Serological tests are negative in the acute stage and are of value only in the chronic cases when the organism has produced ulceration of the intestine. Mild, moderate and fulminating cases occur and some become chronic. Shiga infections tend to be more severe than Flexner or Sonne cases. The stools may contain visible sloughs and then the prognosis is serious. Hiccup is a fatal sign. The complications include conjunctivitis, nitis, arthritis, neuritis and persistent tachycardia.

Treatment

General treatment

Sulphaguanidine. —A. L. Brewer has used sulphaguanidine in the treatment of seventy-seven patients with bacillary dysentery; there were twenty-six acute and fifty-one chronic cases. In most instances the patients with acute infection had not received any previous treatment; a few had been given castor oil and sodium sulphate. Sulphaguanidine was given by mouth in an initial dose of 7 grammes (105 grains) with subsequent doses of 3.5 grammes (55 grains) four-hourly until the temperature was reduced, the general condition satisfactory and the number of stools five or less in the twenty-four hours. The same quantity of the drug was then given four times a day until the stools were semi-solid with only traces of blood and mucus. Thereafter the administration was made three times a day until two or three days after the stools had become normal; in some of the early cases it was continued only until the stools were free from blood. Adjuvant treatment included the giving of 30,000 units of serum in cases of Shiga infection, bismuth and chalk mixture in the early stages and opium or morphine

to relieve pain. Of the twenty-six patients nineteen recovered promptly. Five needed subsequent treatment by colonic lavage for from two to four weeks. Two patients with very severe infections were given lavage and a second course of sulphaguanidine, to which one responded. The sooner treatment was begun the more quickly was cure obtained. The chronic cases were divided into two groups, in one of which the patients were given an average total dose of 90 grammes, or just over 3 ounces spread over six days, and in the other an average total dose of 160 grammes (5½ ounces) was spread over ten days. All responded to treatment, but healing, as shown by sigmoidoscopy, took place in only 55 per cent of the first group as compared with 77 per cent of the second. The importance of obtaining sigmoidoscopic confirmation of healing is emphasized since, unless the ulceration is completely cured, relapse is to be expected.

Sulphaguanidine and succinylsulphathiazole.—An epidemic of Flexner bacillary dysentery occurred in 1942 at the Eloise Hospital, Michigan, affording to C. J. Smyth, M. B. Finkelstein, S. E. Gould, T. M. Koppa and F. S. Leeder an opportunity to try the effect of sulphaguanidine and succinylsulphathiazole in twenty-eight cases. Positive cultures were obtained from the stools of twenty-six of these patients. In the other two, cultures were negative; one died with bloody diarrhoea and high fever, the other subsequently developed a high serum agglutination titre against *Bacterium Flexneri*. The patients were divided into three groups: (1) six who did not receive any sulphonamide therapy; (2) ten who received sulphaguanidine; (3) fourteen who received succinylsulphathiazole. In the first group four patients died and necropsy was performed in two. In both, small shallow ulcers were present throughout the descending colon and rectum and *Bacterium Flexneri* was cultivated from these ulcers. Of the two patients who recovered, one remained febrile for six days with diarrhoea for three. Stool cultures were negative after the fourth day. The second patient was free from symptoms by the third day but stool cultures remained positive for sixteen days. He was then treated with succinylsulphathiazole and subsequent cultures were negative. In the second group one patient died. In seven patients the temperature fell and in eight the diarrhoea stopped within three days. One patient continued to have diarrhoea for fourteen days and was then treated with succinylsulphathiazole. Stool cultures were negative in five cases by the third day. In only one (the patient afterwards treated with succinylsulphathiazole) were they still positive on the eleventh day. In the third group the duration of fever was the same as in the second group. Diarrhoea was controlled after three days in eleven of the cases. One patient died. The authors conclude that both drugs have some value in bacillary dysentery.

Dysentery and diarrhoea in war-time.—Concluding his remarks on dysentery and diarrhoea in war-time, P. H. Manson-Bahr deals with the treatment of bacillary dysentery. In acute bacillary dysentery he advocates initial large doses of sodium sulphate. Diet is most important; arrowroot should be given (but not much milk), and plenty of fluids (from four to six pints daily); brandy may be added. Blood transfusion is of great value in severe cases. Antidysenteric serum is indicated only in severe Shiga infections; it should be given early and in sufficient amount (80 cubic centimetres). Chronic bacillary dysentery usually responds to colonic irrigation with eusol; some cases require caecostomy. Sulphaguanidine, from 6 to 9 grammes (90 to 135 grains) daily for five days, is highly effective in both acute and chronic cases.

Preventive and specific measures.—At a meeting of the Royal Society of Tropical Medicine and Hygiene, N. H. Fairley and J. S. K. Boyd reviewed the subject of bacillary dysentery in the Middle East during 1940–41. The outstanding features were the low incidence, due chiefly to the absence of any large-scale epidemics caused by the Shiga bacillus such as occurred in the war of 1914–18 and to the mildness of the infection. Measures which have been used to control dysentery are as follows. (1) In forward areas, where it may be impossible to construct trench latrines immediately, troops are instructed to bury excreta. Latrines are fitted with fly-proof covers or are treated daily with disinfectant or larvicide. All patients with dysentery should be evacuated immediately. Food must be protected from flies. (2) In fixed camps kitchens must be fly-proofed and fly traps and other measures for destruction provided. Food should be covered both on the tables and in transit from the kitchens. Fly-proof latrines with automatically closing lids are essential. Kitchen workers must cleanse their hands often, and especially after defaecation; they must report sick promptly if symptoms develop. In 1941 a causal organism was isolated from 8,665 patients. Twelve different organisms were found, the highest percentage belonging to the Shiga-Boyd I group. Complications were uncommon; they included portal pyaemia (one case), pneumoperitoneum (one case), haemorrhage, perforation, chronic peritonitis and systemic complications such as renal failure, toxic arthritis, peripheral neuritis, conjunctivitis, parotitis and pneumonia. Routine treatment included rest in bed, the giving of fluids only in the early stages and regular doses of sodium sulphate or magnesium sulphate for the first five days. Most patients recovered; a few died or passed into the chronic stage of the disease. Serum therapy was employed in some cases and the conclusion was reached that, in severe cases of Shiga infection, refined anti-Shiga serum is a useful adjunct to sulphaguanidine treatment. The latter, owing to limitation of supplies, was reserved for use in proved Shiga dysentery and in cases of other types which were particularly severe or complicated, or which occurred in patients undergoing treatment for some other illness or over forty years of age. Over 500 patients were treated by sulphaguanidine with encouraging results. The drug appears to exert a specific action in both the acute and the chronic stages;

toxaemia rapidly subsides, and damage to the bowel is checked. In chronic cases rapid healing of hitherto intractable ulcers occurred. No case of haematuria or renal blockage was observed. In the discussion subsequent to the reading of the papers R. Cruickshank recommended sulphasuxidine (succinylsulphathiazole) in chronic cases as being more effective than sulphaguanidine. E. R. Boland stated that, in two parallel series of patients treated respectively with and without sulphaguanidine, he did not find any convincing evidence of specific action by the drug. H. J. Smyly had been impressed by its action in a series of ten cases.

Brewer, A. E. (1943) *Brit. med. J.*, **1**, 36.

Caldwell, W. A., and Hardwick, S. W. (1943) *Edinb. med. J.*, **50**, 129.

Fairley, N. H., and Boyd, J. S. K. (1943) *Trans. R. Soc. trop. Med. Hyg.*, **38**, 253.

Manson-Bahr, P. H. (1942) *Brit. med. J.*, **2**, 346.

— (1942) *ibid.*, **2**, 374.

Smyth, C. J., Finkelstein, M. B., Gould, S. E., Koppa, T. M., and Leeder, F. S. (1943) *J. Amer. med. Ass.*, **121**, 1325.

DYSMENORRHOEA

See also B.E.M.P., Vol. IV, p. 353; and Cumulative Supplement, Key No. 367.

Aetiology

Basic causes of dysmenorrhoea

Importance of androgens.—As M. M. Cantor, J. R. Vant, L. C. Conn and M. J. Huston point out, the aetiology of dysmenorrhoea is still obscure, but the theory that it is due to hyperoestrinism and resulting increase of myometrial activity has many adherents. Alternatively, it has been suggested that deficiency of androgen substances may be responsible, leading to comparatively unopposed oestrogenic action. In either case it should be relieved by administration of androgens. The action of the latter is to inhibit uterine contractions and diminish the blood supply to the uterus. Testosterone propionate is given in doses of 5 to 10 milligrams ($\frac{1}{2}$ – $\frac{1}{4}$ grain) on alternate days, starting on the day before the onset is expected and continuing throughout the period during which symptoms are usually experienced. Two to four doses are usually enough. The first menstrual period after this course of treatment is completed may be delayed, scanty or suppressed, but this is of no importance. In some of the authors' cases several successive periods were suppressed and subsequent periods were painless. The risk of masculinization occurring with this method of treatment appears to be small; up to 300 milligrams a month has been given over a period of three months without the appearance of hirsutism or hoarseness. These signs, in any case, are transient and the patient may be assured that they will disappear entirely when the treatment is stopped. Testosterone propionate has also been used by Elinor F. E. Black to treat functional disorders of menstruation, including dysmenorrhoea, and she reports successes in a few cases. On the other hand, she insists that the drawbacks of this mode of treatment must not be minimized. They are as follows. (1) The risk of masculinization. Even slight and transient signs of virilism may produce a profound psychological effect upon the patient. (2) The unknown risks of producing some late endocrine imbalance in years to come. (3) The cost, which still makes testosterone treatment impossible for many patients. (4) The danger of indiscriminate prescribing of hormone preparations without proper examination.

Treatment

Endocrine therapy

Use of oestrogens.—S. H. Sturgis and J. V. Meigs, who have previously reported successful results of treatment of essential dysmenorrhoea with stilboestrol and with oestradiol benzoate, have obtained confirmation of their findings in trials made of a third oestrogen body, oestradiol dipropionate. From their former work it emerged that a painless period followed oestrin therapy only when, as shown by biopsy, the formation of a secretory endometrium was prevented, probably by suppression of ovulation. Apparently the effect of oestrogen when given early in the menstrual cycle is to inhibit the follicle-stimulating hormone so that the young follicle fails to mature and ovulation cannot occur that month. Withdrawal of oestrogen is followed by bleeding which for reasons as yet unknown is painless. If oestrogen is given too late in the cycle, when the developing follicle has ceased to depend upon a growth-stimulating hormone, ovulation is not prevented and pain during the subsequent bleeding will not be eliminated. Oestradiol dipropionate was tried during a period of eighteen months in thirty-three cases of essential dysmenorrhoea, over 260 injections being given. Nausea or other toxic symptoms did not supervene. Approximately 130 menstrual periods occurred after treatment and of these eighty-eight, or 68 per cent, were completely painless. In 11 per cent the pain was still experienced but was less severe. In 20 per cent relief was not obtained. Some of these painful periods, however, were delayed and did not appear until four weeks after the last injection. Such an interval suggests that a complete cycle occurred after the cessation of treatment and these periods should not properly speaking be counted among the failures. In other cases failure was due either to an inadequate dose, to starting treatment too late in the cycle or to both. The dose tried at first was 5 milligrams ($\frac{1}{2}$ grain) of oestradiol dipropionate on the sixth day, repeated on the sixteenth day. Since unsatisfactory results were the rule, a single dose of 10 milligrams ($\frac{1}{4}$ grain) on the sixth day of the cycle was used.

for all but twenty-three of the 260 injections; this dose was found to give consistent results, a painless withdrawal flow occurring about two weeks later. In order that the endometrial hypertrophy which follows repeated stimulation without interruption may be prevented, the endometrium may be allowed to break down and bleed after each injection. Thus an anovulatory period should be produced twice a month by repeating the injection on the first day of each period of withdrawal bleeding. Unfortunately the withdrawal interval is variable, and there is a possibility that the second injection, if given according to this plan, will be too late to be effective. It is better to give three injections, the first on the sixth day after the onset of menstruation, the second ten days later and the third another two weeks later. Thereafter injections are given at intervals of ten days, ten days and fourteen days. The treatment is interrupted and an untreated period allowed to occur every fourth month. Oestrogen therapy is not a cure of dysmenorrhoea but can give symptomatic relief.

EDITORIAL COMMENTARY—Painful Menstruation: Advances in Treatment

Pain in connexion with menstruation was formerly classified into clinical types according to whether (a) the discomfort came on before the bleeding and was relieved when the first traces of blood reached the vulva (obstructive dysmenorrhoea), (b) the pain was present for several days before blood was seen and continued until sufficient had been lost to deplete the pelvis (congestive), or (c) there was pain on the first day of a slight period (spasmodic). The last type is the commonest and especially affects nulliparae under twenty-five years of age; the pain of spasmodic dysmenorrhoea is frequently described as cramping or colicky in character. The unusual type, in which pieces of membrane appeared on the vulval pad (membranous dysmenorrhoea), was regarded as belonging to the obstructive group since it was assumed that the cervical canal offered an obstruction to the passage of the membrane.

Unfortunately the symptoms described by many patients cannot be fitted into any of the above three categories and but little clinical experience is needed to realize that this classification is not one of much practical value. It is unfortunate that the pain of many nulliparae, being described as colicky, has given rise to the widely spread idea that dysmenorrhoea in general is due to irregular uterine contractions which are presumably trying to overcome the resistance of a tight cervical canal. This explains the attempts to treat dysmenorrhoea in general with belladonna or atropine and, when they fail to relieve the patient, to advise dilatation of the cervix. There is not any evidence of irregular contractions, and the absence of muscular hypertrophy after years of dysmenorrhoea makes it highly improbable that any real obstruction to the passage of fluid blood in normal amounts exists in the cervical canal. W. Bickers's (1941) investigations with a kymograph and intra-uterine balloon confirm the observations of other workers that normally the uterine contractions in the follicular phase are of low amplitude, considerable frequency and associated with uterine tonus, whereas during the premenstrual and menstrual phases the contractions are of higher amplitude, less frequency and show less tonus. The tracings from patients who do not have dysmenorrhoea are identical in the premenstrual and menstrual phases, whereas tracings from patients with dysmenorrhoea taken during menstruation show a greater uterine tonus than in the premenstrual phase. A biopsy of the endometrium from these patients showed typical progesterone changes, that is true menstruation was present, hence it appears that an increased uterine tonus is the one definite uterine abnormality which was proved to exist in young women of an average age of twenty-one years who suffered from painful menstruation. Further, Bickers showed that the tracings of the contractions and the presence of tonus were unaltered by the administration of atropine, ephedrine, adrenaline, alcohol and calcium gluconate. Morphine abolished both tonus and contractions but it is, unfortunately, contra-indicated clinically.

Attempts are frequently made to treat dysmenorrhoea by hormones, but usually with little success. Oestrogens are often used, and so the possible value of oestradiol, stilboestrol, hexoestrol and other similar drugs must be considered. One reason advanced for using oestrogens is that the uterus is underdeveloped and that oestrin causes the growth of the uterus at puberty. Against this it may be stated that in the enormous majority of patients submitted to dilatation of the cervix because of dysmenorrhoea, the sound passes the usual distance and there is not any evidence of any hypoplasia. Clinically, oestrogens given in reasonable doses for many months usually produce menorrhagia and sometimes an increase of the pain because of the passage of clots. If a heroic dose is given during the follicular stage, it may react on the anterior lobe of the pituitary gland and inhibit the secretion of prolactin so that the follicle does not rupture, hence luteinization does not occur and any bleeding afterwards is of the metropathic type and therefore free from pain. Anovular menstruation is usually painless, and, according to E. Novak, the reason why many girls do not have pain between the thirteenth and sixteenth years is because the 'menstruation' at first is anovular, but when the follicle ruptures and luteinization causes true menstruation to appear, dysmenorrhoea may commence. Progesterone is a great disappointment because the theoretical considerations which have arisen from its action during pregnancy seem to indicate that progesterone should be sedative to the uterus in dysmenorrhoea. But clinically it usually fails to relieve pain, does not alter the tracing of the uterine contractions, is very expensive and would have to be administered every month. Testosterone even in large doses does not alter the amplitude of the uterine contractions or diminish the tonus; there is also a real risk of its causing the growth of hair on the face and altering the voice if it is repeatedly used.

It seems therefore that a large amount of work by various investigators on the pathology of dysmenorrhoea merely confirms the well known fact that it is very difficult to treat the condition successfully by drugs; accordingly it is worth while considering the physiology of normal menstruation in the hope of finding possible causes of pain in addition to the uterine tonus mentioned above. A brief summary of the physiology is that the ovum ripens under the influence of prolactin A, and oestrogens from the Graafian follicle during the follicular phase cause hypertrophy of the endometrium; after ovulation and luteinization, the progesterone causes the secretory and premenstrual phases. The corpus luteum degenerates shortly before menstruation starts, so the final changes have been regarded as due to the withdrawal of progesterone. This seems to be confirmed by the absence of menstruation when the corpus luteum persists in pregnancy. The final changes are the formation of a subendometrial haematoma which breaks through the degenerate endometrium, and the occurrence of exfoliation of the endometrium in small pieces. According to H. B. Whitehouse, the blood clots in the uterus and is then dissolved by a fibrolysin. Thus the passage of clots through the cervix should indicate either an excess of blood or a deficiency of fibrolysin. It is unfortunately necessary to pass a speculum to ascertain whether abnormally large pieces of endometrium and clots are being expelled through the cervix as examination of the vulval pads is useless, but there are obvious difficulties in making an examination by a speculum on the average young patient during an attack of dysmenorrhoea. According to what we know of the changes taking place during the menstrual cycle, premenstrual pain may be due to some abnormality of the corpus luteum, such as haematoma formation, or to an abnormality of the subendometrial haematoma, such as an increased tension of the haematoma due to the endometrium not yielding and permitting the blood to escape. The pain of 'obstructive' dysmenorrhoea may just as well be due to difficulty in the blood getting through the endometrium as to difficulty in fluid blood passing through the cervix, but the former will not be cured by dilatation of the cervix. Pain during the first day may be caused by too sudden a rush of blood into the uterus distending it with a blood clot that is too big for the fibrolysin to deal with and thus causing abnormal uterine contractions in an attempt to get rid of the intra-uterine blood clot. Pain that is severe on the first day and continues until the end of the period, and even after the vaginal loss has ceased, is almost diagnostic of endometriosis since the blood in the closed cavities cannot escape and the tension in those cavities is only diminished slowly as the fluid portion of the blood is absorbed.

As a safe generalization, it may be said that lateral and especially unilateral menstrual pain is of ovarian origin. If premenstrual, it is commonly due to a luteal haematoma, whereas if menstrual and possibly post-menstrual, it is frequently due to endometriosis, a condition which also often affects the ovaries. It is, therefore, very highly improbable that lateral pain will be relieved by dilatation of the cervix or by giving drugs with the object of controlling uterine contractions; simple analgesics may relieve for a time, and if any operation is performed it should include the inspection of the ovaries and resection of portions containing retention cysts or endometriomatous deposits.

Treatment of dysmenorrhoea with gross pelvic lesions is a matter of dealing with the lesion, that is removal of fibroids and other abnormal growths, but the question may arise whether or not a patient with primary dysmenorrhoea who has a congenital retroflexion requires the position of the uterus to be altered. The retroflexion in such a patient is not a displacement, as the uterus has always been retroflexed, and so relief from the pain is not likely to follow ventrisuspension; pessaries can never rectify a congenital retroflexion in the way that an acquired displacement can be permanently cured by their help. In the case of patients who have apparently normal pelvis, the first consideration is to improve the general health and to get them to go into training by regular exercise such as walking to the office or shop every day—and not by playing squash or tennis until they are over-tired one day a week. The second essential is to get the bowel emptied and not merely open for two days before the period is due to start. When the pain is on, any analgesic which is useful for neuralgia should be tried, and it often helps to add a minim of tincture of capsicum or some ginger to give a feeling of warmth in the stomach. Thus a popular mixture is seven or eight grains of phenazone, a minim of capsicum and peppermint water to one ounce. At the same time an attempt is made to find out what is the probable cause and so to decide whether dilatation is worth trying. It is most undesirable to tell patients that they will be cured by marriage, not only because in most cases it is not within the patient's power to carry out such a suggestion, but also because, if pregnancy should be prevented or not occur, the pain would probably be made worse by sterile marriage. If, however, the patient is married and becomes pregnant it is a different matter. V. B. Green-Armytage's investigations seem to show that semen causes growth of the uterus, and so if this is confirmed it would appear that the use of the sheath is the most undesirable form of contraceptive for patients with dysmenorrhoea.

Hysterectomy has been almost entirely replaced by pelvic sympathectomy since the latter is not so mutilating an operation. Moreover many patients continue to complain of pelvic pain after hysterectomy if the ovaries are not removed. The results of pelvic sympathectomy are good although every patient is not cured by the operation; it is a major surgical procedure and not an easy one to perform.

Mention must be made of a condition which is allied to dysmenorrhoea and which is usually termed 'premenstrual distress', the usual symptoms being headache, irritability, abdominal

distension, nausea, pruritus and swelling of the vulva. J. P. Greenhill and S. C. Freed (1941) report good results from the administration of 15 grains of ammonium chloride thrice daily and starting from ten to twelve days before the expected date of the period. They produce evidence that the symptoms are associated with sodium retention, which explains the benefit from the use of ammonium salts.—CLIFFORD WHITE.

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DYSPEPSIA

See also B.E.M.P., Vol IV, p. 367; and Cumulative Supplement, Key No. 369.

Clinical picture

Symptoms suggesting organic dyspepsia

Gastro-enterology in the Forces.—In his presidential address to the American Gastro-Enterological Association, R. S. Boles argued that the American War Department's present policy of appointing specialists in gastro-enterology to all large military hospitals is likely to prove of great benefit to the Service. In the present war, diseases of the digestive tract hold the first place, by a wide margin, as a cause of disability in the armed Forces of the Allies; as contrasted with the war of 1914–18, in which such diseases came seventh on the list, according to the statistics which have been compiled by the Surgeon-General's office. Peptic ulcer mainly accounts for the above high rate. Unparalleled opportunity arises for clinical research into the reasons for what appears to be an extraordinary increase in the incidence of peptic ulceration. The importance to the gastro-enterologist of adequate training in general and psychological medicine, as well as in his chosen speciality, is emphasized.

Functional dyspepsia and its treatment

Military problems.—The military aspects of gastric disease were the subject of the address by the Chairman, W. L. Palmer, to the Section on Gastro-enterology and Proctology at the 1942 annual meeting of the American Medical Association. Opinions differ as to the incidence of gastric disease among soldiers in the war of 1914–18, but in the present conflict dyspepsia has been called by A. Hurst, alluding to the British Army, the most important medical problem of the war. Experience has been similar in the Royal Navy, in the Royal Air Force and in the Canadian Forces. In a series of 287 patients disabled in the British Army because of dyspepsia, 226 had a proved peptic ulcer and a further twenty-one men probably had ulceration. In 92 per cent the ulcer had been present before the war began. Almost all the patients had lived for years on a relatively strict diet and could not tolerate army food. Psychological factors did not appear to play an important part in their breakdown. From the military point of view the problem is twofold: the doubtful value of accepting dyspeptics for the Forces and the disposal of those who develop dyspepsia after enlistment. In selecting recruits considerable variations exist in the practice of the different medical boards. In Canada gastro-intestinal disorders are responsible for more rejections than any other disability except defective sight. In the United States of America men who are known to have had an active ulcer within the past five years are rejected. Those who develop dyspepsia whilst in the Forces should be given proper investigation and treatment, and in the American Army efforts are being made to establish a section of gastro-enterology in each hospital of 1,000 or more beds. It should be possible to assign a certain number of men with peptic ulcer to limited duties permitting them to continue any necessary dietetic and other treatment. As regards gastritis, the symptoms may bear very little relation to the physical signs shown by X-ray examination and by gastroscopy. Even in ulcerative gastritis symptoms may be insignificant. On the other hand, in a recent series of fifty-eight cases of dyspepsia in which all other findings were negative, and in which gastroscopy was performed, only about one-seventh of the patients were found to have serious organic changes in the gastric mucosa. The speaker thought that for the present it is best to act on the assumption that chronic non-ulcerative, non-specific gastritis is not a complaint which disables a man from service in the Forces. On the other hand, certain types of ulcerative gastritis may be related to peptic ulcer and patients with such lesions should be placed in the peptic ulceration group. The clinical diagnosis of gastritis, both acute and chronic, is vague and unsatisfactory and the term is often used to cover any case of so-called functional dyspepsia.

Digestive diseases in the Forces

Incidence, prophylaxis and treatment.—J. L. Kantor surveys the available evidence relating to digestive disease and military service. For his peace-time figures he is indebted to the annual reports of the Surgeon-General of the United States Army, which show that even under peace-time conditions digestive diseases are of considerable importance. The year 1940 is typical of the last decade. The sick rate for diseases of the digestive system was 0.2 per 1,000 strength, and such diseases caused 27 per cent of all deaths from disease. They ranked third as a cause for admission to sick report, fourth as a cause of death, fifth as a cause of discharge for disability and third as a cause of loss of time. The types resemble those encountered

in civil life. The incidence of duodenal ulcer has increased in the Army as it has in the civil population: in 1930 the admission rate for duodenal ulcer was 1.1, in 1939, 1.6, an increase of 50 per cent. In 1940, although the admission rate did not reach 1.6, duodenal ulcer ranked above all other digestive diseases as a cause for discharge. Information regarding digestive disease in armies during war-time is obtained chiefly from foreign sources. During the war of 1914-18 the admission rate for diarrhoea and dysentery varied greatly. In the British Army during the Dardanelles campaign it reached 253.94, with a death rate of 6.93 per thousand. In the present war, during the Polish campaign, 1,200 cases of dysentery occurred among the German troops, with a death rate of 3.3 per cent. In the British Army peptic ulceration shows a high incidence varying from 35 to 55 per cent of the gastro-intestinal cases. The incidence of ulcer perforation among civilians appears to have risen during heavy air raids. Thus in sixteen London hospitals from January, 1937 to August, 1940 the monthly average of perforations was 23. In September and October, 1940 the monthly average rose to 64. Digestive neuroses originate for the most part probably in civil life and occur in the same proportion in the Army. Of gastro-intestinal cases admitted to military hospitals a proportion, stated by some observers to reach 35 per cent, is functional in character. The incidence of gastritis is undetermined since the term is often used loosely to cover any functional dyspepsia. Gastroscopy is essential to exclude gastritis. Malingering appears to be uncommon. Prophylaxis of digestive diseases from the military point of view demands exclusion of dyspeptic patients from the Forces, immunization against typhoid fever and cholera and general hygienic measures to prevent food infection. Doubtful cases among recruits to the American Army are admitted to hospital for a few days for study. Treatment should be given in special gastro-enterological units staffed by specialists, to which patients can be sent from the field hospitals. Considerable progress has been made in this direction in the American Army. Evidence suggests that one-third or more of soldiers developing digestive disease on active service will have permanent digestive disability.

EDITORIAL COMMENTARY—Present-day Aspects of Dyspepsia

Dyspepsia has had more impact on the war than the war has had on dyspepsia. Apart from the possibility that the incidence of gastric ulcers is tending to increase slightly at the moment, it has been notable that neither in the Forces nor in the civil population has there been any increase in serious dyspepsia. Pre-existing ulcers have tended to flare up (1) in the Forces because the difficulty of dieting has led to severe relapses, and (2) in the civil population because the stress of air raids leads to an increase of haematemesis. This is only to be expected from the effects of the physical and psychological stresses of war on people with peptic ulcers.

Minor dyspepsias are causing trouble, and are naturally attributed to food, but the evidence suggests that, although an unaccustomed heavy diet may cause temporary dyspepsia in the Forces, both there and in civil life it is psychological factors which make the dyspepsia the occasion of disability. It is noteworthy that the attribution to war-time diet is lessening, especially among civilians, in whom an initial dislike of wholemeal bread, for instance, is giving place to an acceptance through habitual use. Peptic ulcer causes a large wastage of man-power in the Forces, but the proper diagnostic procedure and the decisions about the disposal of dyspeptics have now been settled and ulcers are less of a trouble to medical officers than minor dyspepsias. The same is largely true in civil practice, in which the ulcer patient often manages to look after himself and carry on with his work, whereas the minor dyspeptic is less satisfactory both to himself and to his doctor.

The key to the whole problem seems to be that it is the patient's whole make-up, body and mind, which determines the effect of his dyspepsia, rather than his stomach or its lesion. The man who wants to rise superior to his difficulties often succeeds, whereas the half-hearted man succumbs, and it is in the psychological handling of dyspeptics that the doctor feels himself (and often is) least adequate. How far psychological factors actually cause dyspepsia, organic or functional, is still uncertain, but the view that emotional states can cause peptic ulceration is undoubtedly gaining ground. There has been in the past a great deal of work done in an attempt to show that psychological factors may contribute to the genesis of ulcers; a start has now been made on the investigation of the actual processes by which the mind influences the function of, and hence the production of anatomical lesions in, the stomach.

There is no doubt, now, that there is such a thing as 'nervous dyspepsia', both in the sense of a neurosis in which the patient seizes on gastric symptoms, and in the sense of an emotional interference with the normal behaviour of the stomach. We do not yet know what kind of emotional disturbance leads to an ulcer, and what kind leads to nervous dyspepsia, but it is clinically helpful that the patient with an ulcer tends to be of the striving energetic type and a most useful member of society, whereas the 'nervous dyspeptic' tends to be feckless, unstable, incapable of keeping to one job for any length of time, and is often unemployed for long periods. The recognition of the two types, which is easy when a careful history is taken, is a help not only in making a diagnosis, but still more in indicating how to handle the patient. The war, with its difficulties in arranging elaborate investigation, has emphasized what has always been known but not always so well realized, that the essence of the diagnosis of dyspepsia lies in the careful eliciting of a history. The history includes two things; the account of the present symptoms and the story of their evolution in time. Present symptoms are more important in the patient's mind, and the doctor is apt to be misled into agreeing

with him. It is their evolution which is important, and that involves a long-suffering but firm orientation of the patient's mind.

With regard to treatment there is a delusion that the war has made it much more difficult. This is untrue. Certainly it is impossible to indulge in dietetic fads, but so long as bread (which can be converted into thin dry toast), potatoes and green vegetables (which can be sieved) are not rationed and there is a sufficiency of butter or margarine, there is not any difficulty in providing enough nutriment in a suitable form. Milk and eggs are pleasant, but not essential. For drugs, magnesium is in short supply, because the import from Germany now takes the form of incendiary bombs but magnesium trisilicate was found, in a large-scale investigation, to be only 57 per cent as efficient as a mixture of magnesia and chalk, which needs less of the metal for its manufacture and the proportions of which can easily be adjusted to suit the laxity of the patient's bowels.—C E NEWMAN.

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DYSPEPSIA, CARBOHYDRATE INTESTINAL

See also B E M P., Vol. IV, p 370; and Cumulative Supplement, Key No 370

Aetiology

Flatulence and war

Aetiological importance of air swallowing.—R. Coope dealing with recent trends in gastro-enterological treatment points out that though no epoch-making advances have been made, war-time conditions, by bringing about changes in people's way of living and shortage of certain drugs, may have done good by purging gastro-enterological therapeutics of fads and fussiness. In Great Britain, as in other countries, dyspepsia has become the outstanding medical problem in the Forces. The fact that service conditions are too strenuous for patients with organic dyspepsia has brought to light an unexpectedly large number of cases of peptic ulcer and gastritis. Among the civil population in frequently bombed cities also, the incidence of perforated ulcer and of haematemesis appears to have increased appreciably during periods of heavy air raids; relapses among subjects of gastric and duodenal ulcer seem to have become more frequent. Flatulence, always a common complaint, is more common in war-time than in times of peace. Before blaming war food, especially the bread, as is often done, it should be recollected that fermentation of ill-digested food is the least frequent cause of flatulence. Air swallowing is far more often responsible, and the commonest determining factors, in the absence of congestive heart failure, cholecystitis or obvious lesion of the digestive tract, are neurosis and chronic constipation. Treatment of the patient's general condition is important but often difficult in war-time and must if necessary be supplemented by symptomatic treatment, for which prosthigmin bromide tablets, 15 milligrams ($\frac{1}{4}$ grain) four times daily, are of value.

Clinical picture

Clinical manifestations

The five main groups—H. Cohen divides the clinical manifestations of flatulence into five groups: belching, passage per rectum of excessive amounts of gas, bloating, that is a feeling of distension; borborygmi; pain or discomfort relieved by expulsion of gas. The amount of gas present in the alimentary tract is the resultant of two factors, entry and absorption. The sources of gases are as follows. (1) *Swallowed air*. In normal people little air is swallowed. If meals are hurried, if mastication is difficult or if salivation is excessive the amount is increased, and certain articles of diet such as *soufflés*, omelettes and, to a greater degree, aerated drinks may carry air into the stomach. The commonest origin, however, is some epigastric or sub-sternal discomfort, which may be a manifestation of some serious disease or on the other hand a trivial symptom which, particularly in neurotics, may start a habit tending to persist after the cause has disappeared. Possible organic causes must be diligently sought and when they have been excluded the other factors mentioned must be eliminated. Meals should be dry and taken more slowly; salivation should be diminished by giving belladonna; the nervous system should be damped by small doses of sedatives. In cases of pure neurosis some little device to prevent swallowing of air may be useful: for instance a cork or large cigarette-holder held between the teeth. Preliminary explanation is necessary but exhaustive psychoanalysis is not advised. (2) *Chemical changes resulting in gastric or intestinal fermentation*. Two main types have been differentiated, intestinal carbohydrate dyspepsia and protein putrefaction. The first type is associated with nocturnal discomfort and passage of excessive flatus and sometimes with loose, malodorous but not putrescent stools. Starch granules with their cellulose envelopes intact are found in the faeces. Roughage is probably responsible. In the second group the stools are alkaline and putrid, and contain undigested meat fibres and large quantities of Gram positive organisms. Products of putrefaction are also excreted by the salivary glands, as may be shown by a dark stain on the dentures. Adjustment of diet is necessary in both types: in the first, cereals and vegetables, especially root vegetables, are forbidden; in the second a lacto-vegetarian diet is prescribed. Intestinal antiseptics are valueless; hydrochloric acid and digestive enzymes are of doubtful value. Any cause of stasis, such

as organic obstruction, encourages fermentation. (3) *Direct excretion from the blood stream into the alimentary tract.* This possibility is as yet unproven. The factors upon which absorption depends are as follows. (a) The nature of the gas. Carbon dioxide is absorbed very rapidly, oxygen much more slowly, nitrogen hardly at all. Methane is absorbed fairly rapidly. (b) The condition of the bowel. Absorption may be diminished as the result of toxic or inflammatory changes in the mucosa or of interference with the intestinal circulation due to local or general causes. Damage to the mucosa is frequently due to purgatives or may result from disease. Treatment, which may have to include surgery, must be directed to the removal of the cause. Carminatives and adsorbents may be helpful as symptomatic remedies, or the flatus tube may give relief.

Flatulence in different forms

Discussion of various causes.—W. C. Alvarez emphasizes the importance when a patient complains of flatulence of finding out exactly what he means, whether belching, abdominal distension, a feeling of gas being trapped in a part of the intestine, or passage of much flatus per anum. Flatulence results much less often from gas formed by fermentation in the bowel than from nitrogen in swallowed air. Some of the gas in the intestine is apparently excreted from the blood, and this excretion may greatly increase under the influence of emotion. Carbon dioxide and oxygen are rapidly absorbed by the bowel. Any condition which interferes with the intestinal circulation is likely to produce gaseous distension, as may pneumonia, which interferes with loss of gases from the lungs. When a patient suffering from such condition is made to breathe pure oxygen the steepening of the gradient in nitrogen tension from the intestine through the blood to the alveolar air results in rapid loss of gas from the distended bowel. Swallowed air usually passes rapidly and painlessly through a normal bowel but gas resulting from eating some food to which a patient is allergically sensitive may remain for hours in segments of the bowel which are in a state of tonic and painful contraction. A single belch is usually due to a reverse wave coming up the oesophagus, but repeated belching is always due to swallowed air, which goes down as far as the cardia and is then returned. It is not enough to tell a patient that he is swallowing air, an attempt must be made to find out why he adopted the habit. Sometimes it is a nervous manifestation, but occasionally, especially in elderly men, incipient heart failure from hypertension or coronary disease may be producing distress round the cardia. Abdominal bloating is usually found in nervous women, and is sometimes due to angioneurotic oedema of the bowel. A false feeling of flatus may occur in connexion with duodenal ulcer or constipation. Excessive flatus may be due to swallowing of large quantities of air or to fermentation. Foul gas is likely to result from the latter cause, especially from eating some food to which the patient is allergic. Some of the worst gas producers are foods not ordinarily considered indigestible, for example milk and eggs. A diet containing much roughage may produce flatulence in sensitive people. Other causes include overeating, anxiety or pain, cholecystitis, incipient coryza, diarrhoea, haemorrhoids, partial intestinal obstruction, intestinal parasites and mild cyclic insanity. It follows that exhaustive examination must precede treatment. Any obvious cause must be dealt with. Symptomatic relief may be given by carminatives. In bad cases a teaspoonful of camphorated tincture of opium is advised. When the gas is in the colon an enema may give relief. Walking about is sometimes helpful because it starts gas moving along the bowel; sipping of water may have the same effect. If allergy to a particular food is suspected an elimination diet may reveal what it is. Avoidance of roughage may help.

EDITORIAL COMMENTARY—Flatulence and its Interpretation

By flatulence is meant the presence of excess of gas in the alimentary tract. It is remarkable that even intelligent laymen often have so little knowledge of anatomy that they picture their food fermenting in a single cavity, from which gas can escape either upwards or downwards. Actually gastric and intestinal flatulence require separate consideration.

Gastric flatulence.—The normal absence of stasis and presence of free hydrochloric acid prevent fermentation in the stomach. Severe gastric stasis, even in the presence of free acid, leads to putrefaction of proteins and fermentation of carbohydrates, but achlorhydria by itself has no such effect. Belching of foul-smelling gas and especially sulphuretted hydrogen is pathognomonic of pyloric obstruction, not necessarily malignant. Belching of odourless gas is always the result of aerophagy. This is generally caused by misinterpretation by the patient of a feeling of epigastric fullness, which he ascribes to wind but is really due to some other cause, such as nervous dyspepsia or gall-bladder disease. In attempting to ease himself by eructation he swallows air and so produces true flatulent dyspepsia which is finally relieved when the swallowed air escapes. Treatment of the underlying cause of the dyspepsia together with explanation of the associated aerophagy generally results in the patient rapidly overcoming what is often nothing more than a bad habit which has persisted after the disappearance of the initial cause.

Intestinal flatulence.—Intestinal flatulence leads to discomfort in the lower part of the abdomen. This is often accompanied by borborygmi and is relieved by the passage of odourless flatus. It is often associated with an accumulation of gas in the highest point of the colon, the splenic flexure, the distension of which causes discomfort beneath the left costal margin. As this is mistaken for gastric distension it often leads to aerophagy, which explains why the patient passes wind in both directions. When the patient lies down at night the gas moves from the splenic flexure to the rectum, from which it is easily expelled.

Intestinal flatulence is the main symptom of intestinal carbohydrate dyspepsia, a very common condition at all ages. It is a result of deficiency of diastatic ferment in the small intestine. Starch contained in the cells of root vegetables, the cellulose walls of which are softened but never ruptured by cooking, is insufficiently digested in the small intestine. On reaching the caecum the diastatic ferments present in the colon penetrate the cells and digest the starch. The sugars produced diffuse into the surrounding soft faeces, where they ferment before there is time for them to be absorbed, as bacteria are present in enormous numbers in contrast with their almost complete absence from the small intestine. The distension of the colon produced by the resulting carbon dioxide causes discomfort, and the organic acids formed at the same time may irritate the mucosa sufficiently to give rise to continuous or intermittent diarrhoea. The stools contain many starch granules which stain black with iodine, but no meat fibres or excess of fat, and on incubation odourless gas is produced in contrast with the absence of fermentation in normal faeces. Excess of enterococci are found on culture, but this is secondary and not a result of infection, as treatment by restriction of root vegetables, rice and porridge, but not of bread and other foods made from prepared starch, results not only in complete relief of the lower abdominal discomfort and diarrhoea but also disappearance of the excess of enterococci. Provision of extra diastatic ferments has little effect, but charcoal absorbs some of the excess of gas when fermentation is not completely overcome by diet. The dietetic restrictions may have to be permanent, but in early cases it is often possible to allow gradually increasing quantities of starch until the diastatic activity of the intestinal juice is fully restored.

In about 50 per cent of cases of intestinal flatulence starch digestion is normal. In these the excess of gas is the result of deficient absorption. This may be due to congestive heart failure or portal obstruction, intestinal flatulence being often the first symptom of heart failure and of cirrhosis of the liver. It also results from the more localized venous obstruction caused by partial volvulus of a very movable caecum, of a redundant hepatic flexure or, most frequently, of a redundant pelvic colon. The last is a comparatively common condition, although it is rarely followed by a complete volvulus and acute intestinal obstruction. These conditions are quite unaffected by restriction of carbohydrates or the use of diastatic ferments. They are aggravated by aperients, but controlled to some extent by keeping the stools soft by means of a vegetable mucilage such as isogel. When, as often happens, the intestinal flatulence causes considerable discomfort and occasional attacks of severe pain owing to partial obstruction by a temporary exaggeration of the volvulus, great difficulty is experienced in getting rid of the flatus. In such cases as mentioned above a subcutaneous injection of pitressin gives complete relief within a few minutes; the bowels are completely evacuated by a single mass peristaltic wave, which carries with it all the gas present in the colon. The patient finds by experience the smallest dose required for the purpose—often only three or four units. This should not cause colic or other unpleasant symptoms. In some cases the patient is comfortable only so long as he gives himself an injection of pitressin every morning.

Lastly, intestinal flatulence may be the primary symptom of carcinoma of the colon, especially when the discomfort or pain is localized in one part of the abdomen and associated with a gurgling sensation in the same position. Carcinoma should always be excluded before making any other diagnosis if intestinal flatulence develops as a new symptom in a patient over the age of thirty-five.—ARTIUR HURST.

Alvarez, W. C. (1942) *J. Amer. med. Ass.*, **120**, 21.

Cohen, H. (1938) *Trans. med. Soc. Lond.*, **61**, 183.

Coope, R. (1942) *Practitioner*, **149**, 277.

DYSPHAGIA

See also B.E.M.P., Vol. IV, p. 377.

Causes of dysphagia

Nervous disorders of swallowing

In a paper read before the Royal Society of Medicine (Laryngological Section) A. Hurst spoke of nervous disorders of swallowing, grouping them as follows. (1) Hysterical dysphagia; this is very rare and yields to simple explanation and suggestion. (2) Dysphagia in organic nervous diseases, resulting from paralysis of the voluntary muscles of the bucco-pharyngeal cavity. The oesophagus and cardiac sphincter are never involved. Paralysis of this kind may occur in faucial diphtheria, usually about the second week; in the motor neurone disease which includes progressive muscular atrophy and amyotrophic lateral sclerosis; in progressive bulbar palsy; and in myasthenia gravis. Acute bulbar paralysis may result from haemorrhage or acute inflammatory lesions involving the nucleus ambiguus. In cases belonging to this group the foods most easily swallowed are of the porridge type, since fluids require more rapid and solids more powerful action. (3) Paterson's syndrome, that is upper dysphagia with anaemia in women. This is by far the most common cause of upper dysphagia. It occurs in about 15 per cent of cases of the simple achlorhydric anaemia common in women of middle age, and is associated with atrophy of the mucous membrane of the tongue and pharynx, cracks at the corners of a stiff, narrow mouth, loss of teeth and spoon-shaped, brittle nails. The pharyngo-oesophageal sphincter is particularly involved, failing to relax to allow food to pass, or even going into spasm. If the anaemia is not promptly treated mechanical obstruc-

tion from fibrosis and contraction may be added to the neuro-muscular disorder. Carcinoma may develop in the atrophied tissues, which explains why post-cricoid carcinoma of the oesophagus is so much commoner in women than in men. (4) Achalasia of the cardiac sphincter, the commonest nervous disorder of swallowing. The existence of an anatomical as contrasted with a physiological sphincter here has been disputed, but is not material so far as the pathogenesis is concerned. The obstruction results not from spasm but from failure of relaxation. Secondary dilatation and hypertrophy of the oesophagus ensue. Evidence has been obtained that the condition results from organic disease of Auerbach's plexus. It is best treated by the passage of mercury bougies.

Hurst, A. (1943) *J. Laryng.*, **58**, 60.

DYSPHONIA

See also B.E.M.P., Vol. IV, p. 384.

Spastic dysphonia

Aetiology

Functional hoarseness.—Hertha Tarrasch defines functional hoarseness as a symptom-complex caused by an incorrect phonatory mechanism; she excludes hysterical aphonia. The entire respiratory apparatus is involved, including the accessory sinuses. The condition is caused by incorrect use of the voice, and this in its turn may be the sequel to acute laryngitis—in which attempts to force phonation have resulted in the formation of bad habits—or it may be due to lack of teaching or to wrong teaching of breathing and voice production. The objective signs include an open glottis in phonation, relaxation and irregularity of the vocal cords, redness or thickening of the cords (not always present) and tenseness of the cervical and facial muscles. A strong emotional component is a feature of such cases. Treatment is a matter of voice training; the patient must be taught to breathe correctly, to close the open glottis and to pitch the voice properly. Exercises are described for accomplishing re-education.

Tarrasch, Hertha (1942) *Arch. Otolaryng.*, *Chicago*, **36**, 53.

EAR DISEASES

See also B.E.M.P., Vol. IV, p. 402; and Cumulative Supplement, Key Nos. 374–384.

Acute otitis media

Treatment

Routine sulphonamide treatment.—As a result of several years' experience in treating acute otitis media by sulphonamides, H. G. Tobey suggests the following routine. Patients are kept in bed and, if possible, in hospital. Sulphadiazine is given in doses sufficient to maintain a blood concentration of at least 10 milligrams per 100 cubic centimetres, and administration is continued for seventy-two hours; at the end of this period the report on the culture is likely to be available. According to the patient's progress administration of the drug is then omitted or is continued in the same or in reduced doses for a period not exceeding ten days. Otherwise the compound is changed for another sulphonamide, that is sulphanilamide for streptococcal, sulphapyridine or sulphathiazole for pneumococcal and sulphathiazole for staphylococcal infection. Sulphonamide treatment carries certain risks as follows. (1) The drugs may have toxic effects which are responsible for a low but certain mortality; (2) they may hinder the development of immunity; (3) there is the possibility of sensitization, which occurs in from 10 to 15 per cent of patients; (4) symptoms of progressive infection tend to be masked. Since otitis media resolves without complications in about 90 per cent of cases, the foregoing objections are weighty, and the author is unable to show that the treatment reduces the number of mastoid operations performed, which he regards as the best criterion of successful treatment.

Chronic suppuration of the middle ear

Complications

Facial paralysis.—K. Kettel discusses facial paralysis associated with acute or chronic suppurative otitis media, basing his remarks upon a series of 264 patients, 169 of whom have been re-examined after periods ranging from one year to thirty-one years. He points out that in a great number of cases of this kind the paralysis disappears after the causative aural disease has been adequately treated and that the chief problem is to decide whether the paralysis is likely to subside spontaneously or whether surgical intervention is advisable. The criterion for this decision is the result of the faradic test: if the reaction is preserved spontaneous recovery may be expected. If operation is decided upon the selection of method turns upon the response of the facial muscles to galvanism. If they still contract the choice lies between infratemporal operation (decompression, suture of nerve ends or nerve transplantation) neurotization—that is attempts to make neurofibrils from pedicled muscle flaps grow into the paralysed muscles—and nerve anastomosis. The results of the infratemporal operations are by far the best. If the facial muscles fail to respond to galvanism plastic operations may be used to correct deformity; the movements of the face cannot be restored. The frequency of facial paralysis is greater in chronic than in acute otitis media. In the present series the number of patients in whom the condition was acute was ninety-six and the percentage of the total admissions in which this complication was developed was 0.97. The number of cases

associated with chronic disease was 168 and the percentage in which facial palsy developed of the total cases admitted was 5.20.

Kettel, K. (1943) *Arch. Otolaryng.*, Chicago, **37**, 303.

Tobey, H. G. (1942) *Ann. Otol.*, etc., St. Louis, **51**, 945.

ELECTROTHERAPY

See also B.E.M.P., Vol. IV, p. 490; and Cumulative Supplement, Key No. 389.

Direct current

Ionization

Chemotherapy by iontophoresis in ophthalmology.—The problem of chemotherapy in ophthalmology is the problem of achieving an adequate concentration of the drug in the ocular fluids and tissues. J. L. Boyd has investigated experimentally the use of sodium sulphathiazole introduced by iontophoresis. A 5 per cent solution was used at room temperature with anion electrolysis. The kathode consisted of a Birkhäuser tube electrode shaped to fit the cornea of the experimental animal (rabbit), the indifferent electrode was placed on the leg. Controls were treated by corneal baths in which the same solution was used without the electric current. A current of from 1 to 5 milliamperes was applied for from two to ten minutes and the concentration of free sulphathiazole in the cornea, aqueous humour and vitreous humour was determined from half an hour to two hours later. Local anaesthesia with combined basal narcosis was used in the earlier experiments, but the local anaesthetic was found to confuse the colorimetric readings and, in the later experiments, ether was given. It was found that, with a current of 1 milliampere for two minutes, the sulphathiazole content of the cornea and aqueous humour was three times as great as when the corneal bath alone was used for the same length of time; with a current of 2 milliamperes the concentration in the cornea and aqueous humour was nine and ten times respectively that resulting from the corneal bath. The concentrations in the vitreous humour were too small and erratic for comparison. The concentrations increased, although not proportionately, with increased strength and duration of current. Damage to the structures of the eyeball was not observed unless a current of more than 3 milliamperes was applied for more than five minutes. It is unnecessary to use a current of more than 1 milliampere for longer than two minutes to obtain a concentration of sulphathiazole which would be effective against ocular infections by organisms susceptible to the action of sulphonamide drugs.

Boyd, J. L. (1942) *Arch. Ophthalm.*, N.Y., **28**, 205.

EMPHYSEMA OF THE LUNGS

See also B.E.M.P., Vol. IV, p. 508.

Chronic obstructive emphysema

Clinical picture

Advanced bullous emphysema.—Under the title of 'the vanishing lung' S. T. Allison reports a case of unusually advanced bullous emphysema. The patient, a well-to-do man, aged forty-one, was first seen during an attack of acute bronchitis, with cough and dyspnoea, of two days' duration. He stated that for a year he had been increasingly short of breath on exertion and unable to sleep on the left side without coughing and becoming breathless. He had had two attacks of pneumonia in childhood and for years had had a chronic cough, probably the result of heavy smoking. No other factor of aetiological importance emerged from the history. Examination showed a fat man (13 stone 8 pounds) with slight cyanosis and dyspnoea. The chest was of normal shape and was resonant throughout, breath sounds were absent except at the left base and bronchitic râles were heard all over the left lung. X-ray examination showed absence of lung markings in the entire right half of the chest, except for a few fibrous strands at the base, and also in the upper half of the left lung field. The functional capacity of the lung tissue still remaining was tested and was found to be remarkably good. The patient was instructed to winter in a dry climate, to avoid strenuous exercise and the abuse of tobacco and alcohol, to reduce his weight by suitable dieting and to wear an abdominal belt designed to elevate the diaphragm and so to increase vital capacity.

Allison, S. T. (1942) *Ann. intern. Med.*, **17**, 139.

EMPHYEMA

See also B.E.M.P., Vol. IV, p. 520; and Cumulative Supplement, Key Nos. 396-398.

Tuberculous empyema

Treatment

Drainage and thoracoplasty.—Three papers by C. Hoyle, W. C. Fowler and R. C. Brock are devoted to different aspects of treatment of tuberculous empyema. C. Hoyle lays down certain broad principles which are to be observed. The high incidence of empyema among patients who have a pneumothorax limited by adhesions, or whose disease is widespread and caseating is a strong reason for discontinuing a pneumothorax which cannot be made satisfactory. In established empyema treatment should be governed by the presence or absence of secondary pyogenic infection. When it is present aspiration is very seldom beneficial; it fails to keep the pleural cavity empty, rarely controls toxæmia for long, and is associated

with considerable risk of infection of the chest wall. Drainage at the earliest possible moment is the proper treatment, even although the outlook is dark, unless the state of the other lung or of the chest wall allows of a thoracoplasty within a short time; without drainage the mortality rate approaches 100 per cent. When pyogenic infection is absent repeated aspiration with lavage sometimes succeeds in arresting the pleural disease but, if it fails, thoracoplasty in stages is the best treatment, provided that the state of the other lung and of the patient permits it. W. C. Fowler thinks that the introduction of oxygen into the pleural cavity encourages the activities of the tubercle bacillus and the formation of an empyema, pointing out that this complication has become much more common since artificial pneumothorax treatment was introduced. The treatment of tuberculous empyema is best accomplished by obliterating the space between the layers of the pleura. The bacilli are then reduced to living in a medium with a relatively low oxygen tension. The space may be obliterated either by re-expansion of the lung or by thoracoplasty. Every patient with tuberculous empyema should be treated from the start as though thoracoplasty would be required eventually. Hence needling should always be done with great care and well away from the field of a possible operation for, if improperly done, needling may leave debris in the pleural cavity or cause the formation of a sinus which at best interferes with subsequent thoracoplasty and at worst admits secondary infection to the pleural cavity. The proper procedure is to puncture the chest well above the level of the fluid and to introduce a catheter through the canula down to the bottom of the pleural space. By such means masses of debris can be sucked up and thoracoscopy may be performed afterwards to ensure that the cavity is empty. Dakin's solution may be left in the cavity. R. C. Brock gives the results of treatment in ninety cases of simple tuberculous empyema and in eighty-four secondarily infected cases. In the first group the mortality without thoracoplasty was 77 per cent, and with thoracoplasty 14 per cent. In the second group the mortality was 91 per cent without thoracoplasty and 29 per cent in those who had the operation. The writer advocates drainage, with thoracoplasty as soon as possible afterwards, that is within a matter of days, in every case in which the condition justifies it.

Brock, R. C. (1943) *Brit. J. Tuberc.*, **37**, 18.

Fowler, W. C. (1943) *Brit. J. Tuberc.*, **37**, 14.

Hoyle, C. (1943) *Brit. J. Tuberc.*, **37**, 10.

ENCEPHALITIS EPIDEMICA

See also B.E.M.P., Vol. IV, p. 546; and Cumulative Supplement, Key No. 399.

Aetiology

The virus

Characteristics of the virus.—During an epidemic of encephalitis in North Dakota and Minnesota in 1941, E. C. Rosenow studied the brains of human beings and of various kinds of animals which died from disease, from fifty-five emulsions a neurotropic type of streptococcus was isolated. The emulsions were used to inoculate guinea-pigs and mice, and 52 per cent of the animals succumbed to encephalitis. The streptococcus was also demonstrated in material such as dust and water, including air samples taken at a height of 2,000 feet above the epidemic zone. Inoculation of animals with cultures obtained from these sources caused death from encephalitis. Encephalitis also resulted when animals and fish were caused to inhale the streptococcus. Characteristic encephalitic lesions and virus were found in the brains of animals which had died of encephalitis, occurring either spontaneously or after inoculation of streptococcus-containing material or of virus derived from the streptococcus. The virus from these brains invariably produced encephalitis on inoculation into animals. The theory is advanced that virus represents a filtrable phase of the streptococcus. It is believed that spread by air was a major factor in the evolution of the 1941 epidemic.

Treatment

Chronic stage

The treatment of Parkinsonism.—A. Hall describes the treatment of the disabilities of chronic Parkinsonism. Disturbances of mobility can be relieved, often greatly, by drugs of the atropine class given in sufficiently large dosage. Automatic movements may be freer at night and it may be desirable to readjust the patients' mode of life, for instance in regard to meals, so as to take advantage of this release of inhibition. The gait may be improved by the aid—probably mainly psychological—of some slight support such as a Taylor's brace. Tremor and eye-closure attacks are not affected by atropine. Drooling can be stopped by atropine administration, or by X-ray treatment of the salivary glands.

Hall, A. (1943) *Lancet*, **1**, 193.

Rosenow, E. C. (1942) *Proc. Mayo Clin.*, **17**, 551.

ENCEPHALO-MYELITIS

See also B.E.M.P., Vol. IV, p. 553; and Cumulative Supplement, Key No. 400.

Toxic encephalopathies

Arsphenamine

Haemorrhagic encephalitis.—Haemorrhagic encephalitis is a recognized complication of treatment with drugs of the arsphenamine group. C. B. Courville and C. Marsh have studied

the cerebral lesions in twelve fatal cases, and conclude that multiple bilaterally symmetrical haemorrhagic necrosis of the brain should be regarded as a characteristic manifestation of arsphenamine poisoning; symmetrical cerebral lesions were observed at necropsy in seven of the ten subjects, and tended to involve in particular certain areas of the brain, including the corpus callosum, optic thalamus, external capsule, forceps minor and forceps major. In one case the symmetrical lesions were associated with scattered petechial haemorrhages; in four other cases scattered petechiae only were present. In one case gross haemorrhage had occurred. The tendency to bilateral symmetry of the lesions is explained, in the authors' view, by local dilatation of the vessels which increases their susceptibility to the poison and which accompanies physiological activity of the affected part of the brain.

Courville, C. B., and Marsh, C. (1942) *Arch. Derm. Syph.*, N.Y., 46, 512.

ENDOSCOPY OF THE UPPER RESPIRATORY AND ALIMENTARY TRACTS

See also B.E.M.P., Vol. V, p. 1.

Gastroscopy

Uses and indications

Dyspepsia in the Forces.—A. M. Gill analyses the gastroscopic findings in a series of 1,000 cases in the Forces with a view to determining the value of this form of examination in the assessment of the Service dyspeptic. The Hermon Taylor gastroscope was used throughout. The cases have been divided into three groups according to the X-ray findings. Group A consisted of cases in which X-ray revealed a gastric lesion; even in this group the gastroscope proved to be of practical value in certain cases. In deciding whether or not a gastric ulcer is completely healed gastroscopy is a cheaper and more certain method than X-ray. Gastroscopy is also helpful in the classification of gastritis and in the subsequent observation of the results of treatment. Most superficial and hypertrophic types are not sufficiently serious to incapacitate, and a man can be retained in a low category without having hospital treatment. Mucosal atrophy is usually a permanent progressive lesion and an indication for discharge. Patients with multiple erosions usually respond quickly to treatment but tend to relapse. In sixty cases (four of ulcer, one of ulcer scar and fifty-five of gastritis) gastroscopy failed to reveal the lesion. In the present state of knowledge absence of gastroscopic evidence does not exclude gastritis and should not be allowed to weigh against a positive X-ray. Group B consisted of cases in which the X-ray was negative. Gastroscopy is indicated in any condition of chronic dyspepsia and much diminution of acid secretion, because of the possibility of early development of carcinoma. Group C consisted of cases in which the X-ray demonstrated some abnormality of the duodenum or pyloric canal only. Gastroscopy seldom made any significant contribution to the diagnosis. Instrumentation was unsuccessful in eight and partially unsuccessful in three cases, the causes including oesophageal stricture, lack of cooperation on the patient's part and failure of the light.

Gill, A. M. (1943) *Lancet*, 1, 333.

ENTERIC FEVERS

See also B.E.M.P., Vol V, p. 50, and Cumulative Supplement, Key Nos. 417-419.

The enteric group of fevers

Treatment of the enteric group

Prophylaxis: importance of reliable vaccine.—J. S. K. Boyd compares the incidence of enteric group fevers among British and Axis prisoners of war in North Africa. Information obtained from the British medical officer in charge of a British prisoners' camp shows that in spite of extremely primitive sanitary arrangements and complete absence of facilities for washing no cases of enteric occurred among the 16,000 or more inmates of the camp during a period when the disease was rife among Italian troops in the neighbourhood. On the contrary, among Italian prisoners numerous cases occurred. In spite of inoculation with vaccine of Italian manufacture, which was used because supplies of British T.A.B. were insufficient to meet the sudden demand, an outbreak of considerable magnitude occurred in one camp in the summer of 1941 and cases continued to appear until early in August when adequate supplies of British Army vaccine became available. Two-dose re-inoculation was then performed in the affected camp and after this, although not necessarily as a result of it, the epidemic rapidly waned. In the absence of any other explanation the author attributes the comparative immunity of the British troops to the use of a potent vaccine. Animal experiments confirmed the inefficacy of the Italian preparation.

Typhoid fever

Aetiology

Use of the Vi bacteriophage.—In a report to the Medical Research Council, A. Felix describes the results obtained from the use of Vi bacteriophage in the typing of typhoid bacilli. By this test, devised by Craigie and Yen, it is possible to divide typhoid bacilli into a number of well-defined types. By propagating a particular phage on typhoid strains isolated from different sources it can be made to develop a high degree of specificity against the strain on which it is grown. When such adapted bacteriophages are tested against various typhoid strains it is found that the latter can be classified according to their response to the

different phages and that strains which are related epidemiologically belong to the same phage type. Certain bacilli known as the 'O' form do not contain any Vi antigen and therefore cannot be typed; 'imperfect' forms also occur. These, however, are in a minority. Typing of the typhoid bacillus in this way gives results as reliable as those obtained in the case of streptococci or pneumococci. The test is of great practical value in unmasking the source of infection of sporadic cases and small groups of cases. The material examined yielded bacilli belonging mainly to eight of Craigie's original types.

Treatment

Doubtful results with sulphaguanidine.—Two carriers of the typhoid bacillus have been treated successfully by R. J. Hoagland with sulphaguanidine. Conflicting reports are found in the medical literature concerning the efficacy of this drug in the treatment of typhoid fever carriers. The two cases were as follows. The first was that of a healthy girl of seventeen who had never had typhoid fever. Her father was also discovered to be a typhoid fever carrier. Her faeces were found on four consecutive occasions to contain *Eberthella typhosa* (*B. typhosus*). She was given 2 grammes of sulphaguanidine four times a day for six days. A specimen obtained a week later showed *Eberthella typhosa* still present. A second course of treatment was therefore instituted, 4 grammes of sulphaguanidine being given five times a day for six days. Fourteen consecutive stool cultures taken up to forty-three days after completion of the second course of treatment, during which the blood concentration of sulphaguanidine was 2.48 milligrams per 100 cubic centimetres, failed to reveal *Eberthella typhosa*. The second case was that of a boy aged fourteen, convalescent from a mild attack of typhoid fever. Five consecutive specimens of faeces yielded *Eberthella typhosa*. He received 20 grammes of sulphaguanidine daily for six days, and seven examinations, the last of which was made seventeen days after treatment, were negative. It is possible, however, that the abrupt disappearance of *Eberthella typhosa* in this case was coincident with, rather than due to, the sulphaguanidine treatment. In neither case were any toxic manifestations observed during treatment. The author advocates the use of large doses of sulphaguanidine in the treatment of the carrier state if smaller doses prove ineffective.

Good effect of colloidal tin.—R. Reitter and K. Marberg have investigated the bactericidal effect of tin upon various micro-organisms and its application to the treatment of typhoid fever. A set of experiments was carried out *in vitro* in which 1.0 gramme of powdered metallic tin was prepared in Ringer's solution in each of thirteen tubes. Thirteen control tubes contained Ringer's solution only. Cultures were made of the organisms to be tested and standardized suspensions were prepared therefrom. One tube with tin and one control tube were inoculated with equal amounts of each suspension and incubated for one to ten days. Upon the following organisms tin did not have any effect: *Enterococcus*, *Salmonella enteritidis* (Gaertner), *Pseudomonas pyocyanea*, *Bacillus proteus* and *Bacillus dysenteriae* (Shiga). All the other organisms tested were gradually reduced in number as compared with the controls and eventually destroyed. They included *Pasturella pestus*, *Bacillus typhosus*, *Salmonella paratyphi* A and B, *Staphylococcus aureus*, *Bacillus dysenteriae* (Flexner), *Escherichia coli* and *Brucella melitensis*. Since the susceptibility of typhoid bacilli to tin equalled that of *Staphylococcus aureus* and since tin preparations have been used successfully for certain staphylococcal infections it was decided to try the effect of tin in typhoid fever. The possible toxic effects of the drug were first investigated in dogs. There were not any ill effects after the oral administration of large doses of a preparation of colloidal metallic tin mixed with tin stearate. The tablets were therefore given to patients with typhoid fever in doses calculated according to the patient's age. The course of treatment lasted for ten days; a double dose was administered on the first day. The death rate in a group of 100 severe cases in which tin treatment was used was only 3 per cent as compared with 8.2 per cent in a control group of 482 cases. There were not any toxic effects observed. The duration of the disease appeared to be shortened.

Carriers

Type D4 carrier discovered after two years.—W. H. Bradley describes the first sustained attempt made in England to apply typing with Vi bacteriophage to a field study of endemic typhoid fever. During 1940 the Emergency Public Health Laboratory Service began to concentrate investigations of typhoid cultures in a special laboratory in which a collection of the various phage types of *Bacterium typhosum* was accumulated. Up to the beginning of 1943, twelve types had been recognized as causing disease in Great Britain, including four types or subtypes not previously described. One of these hitherto unknown types, D4, was selected, owing to its presumed rarity, for special study. Whenever it was recovered from a patient or carrier exhaustive inquiries were made. In this way apparently sporadic cases which had occurred over a period of two years were traced to their source. The total number of cases was nineteen and they occurred in widely scattered parts of the country. The only link between them was the milk supply. The patients had obtained their milk from a number of different retailers but the latter had all been supplied from a certain distributing depot; and this again received milk from a large number of farms, at one of which a chronic D4 carrier was discovered.

Paratyphoid fever

Aetiology

Dangers of ram-water.—S. C. Parry gives an account of a small paratyphoid B outbreak

which occurred in Worcestershire in 1941. The first two patients had a common milk supply and when the farm was visited it was found that the machine-milker was suffering from slight symptoms which were subsequently shown to be due to paratyphoid B infection. His young son had been admitted to hospital about a week previously with a three weeks' history of diarrhoea, and a diagnosis of paratyphoid fever was later made. The farm also received milk for bottling from six local producers. Paratyphoid B was absent from all samples of milk, but was found in the ram-water used in the dairy. The milker's son was discovered to have been drinking this water from the gulley outside the dairy in which it flowed. The milker may have caught the disease either from his son or from drinking the water or the raw milk, and the milk may have been contaminated either by him or by the water. One of the sources of the ram-water was close to the outfall of a sewage effluent from a large depot in the district to which much of the milk from the farm in question was sent, and a cook at the depot was found to be suffering from paratyphoid B. As a result of this vicious circle a total of five cases occurred among the employees of the depot and ten others occurred among the customers who obtained milk from the infected source. The course of the outbreak emphasizes the potential dangers of using ram-water in dairying. It is probably more dangerous than ordinary brook water, for it is withdrawn continuously and is therefore more liable to pollution than water taken intermittently from a brook. The amount of dilution undergone by the sewage between its point of entry and the ram was estimated and was found to be less than one in four.

Actiology of paratyphoid fever. B

Defective water supply and infection. —D. J. Jones, P. G. H. Gell and R. Knox describe an outbreak of paratyphoid B which occurred at a village in Northamptonshire. The infection was detected in twenty-one out of thirty-four residents in a group of seven cottages built round a court containing a shallow well from which the water for all the cottages was pumped. Clinical illness occurred in six persons and blood samples from the remaining fifteen gave positive agglutination tests for *Bacterium paratyphosum B*. Most of the fifteen people referred to were found to be excreting paratyphoid B bacilli in the faeces. Only four of the six who complained of illness had typical symptoms. The well supplying the cottages was subject to flooding from surface water in the yard during heavy rainstorms. The pump, situated fifteen feet from the well, was at least fifty years old. The houses round the court were served by four water-closets the sewage from which discharged into pipes running within a few feet of the pipe connecting the well and the pump. *Bacterium paratyphosum B* was isolated from five separate samples of the water. The manner in which the well became infected could not be discovered. After the epidemic, main water was laid on to the houses concerned.

Treatment

Failure of sulphaguanidine —The inefficacy of sulphaguanidine in a series of cases of paratyphoid B infection has been demonstrated by T. F. M. Scott, P. B. Beeson and W. L. Hawley. During an outbreak of the disease a group of forty patients was treated with sulphaguanidine and a control group of forty-eight patients without it. Children under five years of age were excluded from the study. The drug was given for ten days. The daily dose varied according to the patient's age from 8 to 16 grammes (120–240 grains) during the first five days and 4 to 8 grammes (60–120 grains) during the second five days. All patients, including the controls, were made to drink at least 3 litres of water per twenty-four hours, in order to avoid the risk of kidney damage in the treated group. No effect on the course of the disease could be detected as the result of sulphaguanidine treatment, and clearing of the stools from *Bacterium paratyphoid B* was not accelerated as compared with the controls. In a second study a group of twenty-nine convalescents was divided into two subgroups, one of fourteen patients who were treated with sulphaguanidine and the other of fifteen who were used as controls. Again there were not any differences discernible between the two groups. Finally four carriers were treated without the least effect. There were not any toxic effects to be noted.

EDITORIAL COMMENTARY—Some Newer Aspects of Enteric Fevers

As in other intestinal disorders associated with diarrhoea, due regard must be paid in enteric fevers to an appropriate daily intake of fluids, vitamins and sodium chloride. First with regard to fluids, indications of toxæmia become more pronounced if dehydration occurs, and from the outset it is important that the patient should receive an ample supply of fluid. To this end he should be encouraged to drink water between his feeds, a daily total intake (including milk) of 100 fluid ounces or so being aimed at. In severe instances of toxæmia, normal saline solution containing 10 per cent glucose should be given intravenously until the output of urine reaches and is maintained at 50 fluid ounces in the twenty-four hours. Among the articles of food employed to relieve the monotony of a diet of which the chief ingredient is milk, special mention may be made of apple purée which is made by thoroughly cooking and pulping the apples until they are of a consistence similar to that of apple sauce. Apples are rich in pectin and it has been suggested that this substance aids in the healing of ulcers. Secondly it has been suggested that the sequel of post-typhoid neuritis is largely due to an avitaminosis and that when it occurs it should be treated as such. The French observers P. Giraud and A. Valette in an interesting paper on the treatment of typhoid fever in children conclude that vitamin A is of considerable value in preventing hæmorrhage, perforation of the bowel and

skin lesions, but that its employment did not have any effect on pulmonary or cardiac complications or on the duration of the disease. Thirdly it is important that a daily intake of 10 grammes (150 grains) of salt should be secured. Nausea and vomiting are less likely to occur when there is no deficiency of water and when a sufficiency of sodium chloride is included in the daily regimen.

During the present war synthetic cream has been responsible for localized outbreaks of paratyphoid B fever. In most cases infection seems to have taken place at the bakery, at which the cream has been handled by a carrier, rather than at the place of manufacture. For the detection of carriers the Widal test is not wholly reliable, for transient carriers may not show specific antibodies in the blood. It is of limited use as a preliminary measure in tracking infected persons among a large staff of workers but repeated bacteriological examination of faeces and urine must be the chief means of discovering excretors. The new method of typing typhoid organisms according to their reaction to a specific bacteriophage has already borne fruit. By its means, in a small but rather widespread epidemic in the home counties, in which, in all the cases examined, the organisms were found to be of the same phage type, the outbreak was traced to a farmer concerned with the supply of milk who was living a hundred miles away from the scene of the trouble.

As sulphaguanidine has been found to be of use in the treatment of cases of bacillary dysentery it is disappointing to find that it is of little value in the treatment of enteric fever; nor, if it is given in the convalescent stage, does it shorten the period of excretion of the organism. Perhaps this is not altogether surprising, for these diseases are not essentially local infections of the alimentary tract but infections of the blood stream, and experiments with the drug *in vitro* have shown that growth of *B. typhosus* is only moderately inhibited and that of *B. paratyphosus* not at all. An occasional case has been reported from time to time in which a carrier has become free from enteric organisms while taking sulphaguanidine but this is not a usual occurrence.

It has been agreed after theoretical considerations that the combination of an antiseptic with phenolphthalein might prove to be of service in the case of biliary carriers, for phenolphthalein after being absorbed is excreted in the bile (hence the use of sodium tetraiodophenolphthalein in radiography). Some success has attended the giving of soluble iodophthalein in doses of 4 grammes (60 grains) administered by mouth in orange juice three times a week until forty doses in all have been given. The drug is given in the early morning so that the maximum concentration of the drug might be reached at night when rest and the absence of food allow the gall-bladder to remain quiescent, and throughout the treatment a low fat diet is instituted in order to avoid unnecessary contractions of the gall-bladder. In a careful research carried out on these lines in the United States of America a number of successes have been reported. In some of the cases in which the patients still continued to excrete organisms in the faeces, it was found that the bile was sterile, consequently such patients were regarded as examples of true intestinal carriers. They were therefore treated with sulphaguanidine but unfortunately without success. In view of the possibility of a biliary carrier being freed from organisms by soluble iodophthalein a course of treatment by this drug should be carried out before recourse is made to cholecystectomy. —C. E. LAKIN.

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EPIDERMOLYSIS BULLOSA

See also B.E.M.P., Vol. V, p. 82.

Aetiology

Familial incidence

Associated with cancer of the throat.—S. A. Yaffe reports observations on two brothers with epidermolysis bullosa, in a family of five siblings (four males, one female); the two other brothers were also the subjects of epidermolysis bullosa but the sister escaped the disease. One brother died of cancer of the throat. The paternal grandfather, the father and his two brothers suffered from the same disease of the skin. The two siblings reported on by Yaffe are married and their male children all suffered from epidermolysis bullosa. The mother of the five siblings and her sister died from cancer of the throat; it is not stated whether or not they were the subjects of epidermolysis bullosa, but the question is raised regarding the part played by this disease as a factor disposing to oesophageal cancer.

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EPIDIDYMITIS

See also B.E.M.P., Vol. V. p. 86.

Acute epididymitis*Non-gonococcal and non-tuberculous*

E. G. Slesinger, who opened a discussion before a combined meeting of the Surgical and Urological Sections of the Royal Society of Medicine on the subject formerly regarded with cautious scepticism, pointed out that non-gonococcal and non-tuberculous epididymitis is far commoner than text-books would suggest and its incidence in the Forces in the present war is especially high; he gave details of thirty-four cases seen at Preston Hall E.M.S. Hospital, of which eleven were bilateral and six recurrent; the onset was sudden in all cases with pain and swelling, the whole epididymis being enlarged, hard and tender; the vas deferens was thickened in sixteen cases and the vesiculae seminales in twelve. In only twelve patients was the urine abnormal, and then there was a small quantity of albumin and a few pus cells. The condition might be regarded as tuberculous and needlessly submitted to unnecessary operation. Unless there was definite evidence of tuberculosis elsewhere every case should be treated conservatively with rest and local heat. Infection: in one group cure followed in three weeks; in another group it might take three months. D. McGavin recognized three groups of this form of epididymitis—inflammatory, obstructive and vascular; the obstructive and vascular are small and the conditions occur in older subjects. R. H. O. B. Robinson reported on the age and incidence. one patient was under the age of twenty years, sixteen were under thirty, sixteen under forty and fifteen over forty years of age. Slesinger did not consider that sulphonamide drugs affected the course of the disease, and G. L. M. McElligott remarked that non-gonococcal epididymitis is usually unaffected by sulphonamide drugs.

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EPILEPSY

See also B.E.M.P., Vol. V, p. 96; and Cumulative Supplement, Key Nos. 424-432.

Aetiology*Traumatic epilepsy*

Head injuries and electroencephalographic observations.—Opening a Discussion of the Section of Neurology of the Royal Society of Medicine, H. G. Garland pointed out that traumatic epilepsy is much more likely to develop after certain kinds of head injury. Gunshot wounds are outstanding in this respect; thus of a group of 317 cases dating from the war of 1914-18 34 per cent of the men have developed epilepsy, the onset in the majority occurring within the first few months. The reason for the development of epilepsy after other types of head injury is much more difficult to understand; such cases include the 'closed' head injuries due to a blow or fall on the head. Gross focal damage to the brain is rare, the lesions tending to be diffuse or small. Epilepsy develops in a certain proportion, probably about 3 per cent, of these cases; the highest figure claimed is about 20 per cent, the lowest figure represents an incidence considerably below that of epilepsy in the general population. A history of head injury was obtained in 16 per cent of a group of 244 cases of epilepsy in the Forces and, of these thirty-nine cases of head injury, twenty-eight were classified as severe, that is the period of post-traumatic amnesia exceeded three hours. Whether or not patients in whom epilepsy develops after a head injury are those with a constitutional epileptic tendency is not yet clear but, since electroencephalography suggests that such a tendency exists in 10 per cent of the population, this might well account at least for such cases in civilians. W. G. Walter considered the physiological phenomena observed in cases of epilepsy. Electroencephalography shows that the fit is only a part of the epileptic picture; persistent electrical abnormalities are found in many cases of epilepsy, both essential and traumatic. Electrical abnormalities appear to be much commoner in young patients and are almost invariable in children who have suffered birth injury. The changes which occur in the electroencephalogram during the convulsion are always the same, irrespective of the cause of the fit. Records of the *petit mal* type are very rare in traumatic cases and it seems probable that true *petit mal* attacks are never directly or entirely attributable to injury. Evidence has not been obtained that trauma causes a specific type of record; hence electroencephalography does not hold out any hope of distinguishing between the latent epileptic and the purely traumatic case, if this exists.

Water metabolism and epileptic convulsions

The significance of the specific gravity of the blood—The relation between water metabolism and convulsions has been studied in two series of epileptics by T. T. Stone, A. J. Arief and J. A. Luhan. (1) In a group of ten out-patients the specific gravity of the whole blood was determined before and after the subjects had drunk 2 litres of water. Two samples of blood were taken beforehand, and three were taken at fifteen, thirty and ninety minutes afterwards. (2) A second group of thirty-one patients was in hospital for the test. Two whole-blood samples were examined before the water was given, and samples of blood serum were examined at thirty, sixty and 120 minutes afterwards. Each patient received a hypodermic injection of pitressin (pituitary pressor principle) before and after drinking the water. In the first group

the average decrease in specific gravity after ingestion of water was so slight as not to be of any statistical significance; the lowest figures were obtained ninety minutes after ingestion of water. One patient in this series had a fit just after the specific gravity had fallen, at thirty minutes, from 1.0565 to 1.0552. At ninety minutes the specific gravity was 1.0537 and the effects of the attack had almost worn off. No other patient in either series had a fit during the experiments. In the second group of patients the average fall in specific gravity was somewhat greater but still not quite statistically significant. The lowest figure was obtained sixty minutes after ingestion of the water. To determine whether or not the degree of diminution of specific gravity found in the experiments represents an abnormal response on the part of the epileptic, it is necessary to compare it with the dilution occurring in a normal person. The method of determining specific gravity used in the experiments was that devised by H. G. Barbour and W. F. Hamilton.

Mental and physical abnormalities in epileptics

Mental abnormalities

Mental deterioration in organic epilepsy.—A. J. Arieff and G. K. Yacorzynski, having shown that in non-organic epilepsy mental deterioration does not occur even if bromides are given over a period of five years, have periodically applied the Stanford-Binet test to twenty-seven patients with organic epilepsy, to determine whether or not deterioration was present and, if present, to what extent. The cause of the fits was trauma in eight patients, inflammatory disease in eight, tumour in five, vascular disease in four and chronic alcoholism in two. From two to five determinations of the intelligence quotient were made on each patient at intervals of from one to nine years, and the time elapsing between the first and final tests was from one to ten years. An average decrease of 6.0 I.Q. points was found between the first and final tests of the whole group, a significant decrease being observed in 37 per cent of the patients. Three patients showed a significant increase. The patients were also compared with a group of sixty-three non-organic epileptics, and evidence was obtained of deterioration having taken place before the initial test, which gave a mean figure of 74.3 I.Q. for the organic and 85.1 for the non-organic cases. There was not any apparent relation between the different organic causes of the epilepsy and the degree of mental deterioration.

Recent observations on epilepsy

Investigations and electroencephalography.—In a paper read before the American College of Physicians, W. G. Lennox (1943²) deals with recent advances in the knowledge of epilepsy. This disease presents a formidable problem, its victims in the United States of America equalling in numbers the victims of active tuberculosis, and so far little progress has been made in solving it. Twenty years ago, however, an osteopath announced that starvation prevents convulsions, and from this discovery arose the ketogenic diet treatment which simulates starvation and has been found valuable, especially in the treatment of children. The discovery that hyperventilation or ingestion of large quantities of alkalis would precipitate an attack supported the advocates of the ketogenic diet. Seizures were found to be induced also by mild anoxaemia and by alteration of the water balance and of the concentration of various constituents of the blood. Electroencephalography was the next step forward; it has demonstrated the underlying hereditary factors operating in epilepsy. Manifest epilepsy is not inherited, but a predisposition or susceptibility is an hereditary quality. This predisposition can be demonstrated by electroencephalography. Dysrhythmia, on the other hand, is met with not only in epileptics and in persons whose conduct or psychological constitution is abnormal but also in seemingly normal persons, and for all that we know dysrhythmia may accompany high mental achievement. Behind the electrical pulsations of the brain lie the chemical processes of discharging nerve cells, and of these nothing is yet known. Studies of the blood passing through the brain have shown that in normal subjects the respiratory quotient of the brain is 1.0, and that the metabolism of that organ is closely dependent upon that of glucose. In patients with *petit mal* both arterial and jugular blood contain reduced quantities of carbon dioxide; the respiratory quotient is below 1.0 and the brain uses less glucose per unit of oxygen than does the normal brain.

Diagnosis

Differential diagnosis

Electroencephalography.—A. Feiling's Lettsomian lectures on epilepsy begin with a discussion on the diagnostic value of the electroencephalogram. In normal subjects the only part of the brain from which recognizable waves can be elicited is the visual association area. The normal rhythm is called the α rhythm, and has a frequency of about ten waves per second. Many organic lesions of the brain are associated with the appearance of the so-called δ waves, which have a slower rhythm and often a larger amplitude than have the α waves. By taking records from several places simultaneously the source of the abnormal waves can often be found. In epilepsy two abnormalities occur. (1) In many patients a δ rhythm is constantly present between attacks. The focus of origin varies in the different types of epilepsy. This resting abnormality is rare in patients over forty years of age, common in those under twenty. It is increased by a low blood sugar concentration and by overbreathing. (2) During the seizures various abnormal waves are observed, depending upon the type of epilepsy. From the diagnostic point of view a negative electroencephalogram between attacks has not any value; a positive one is strong presumptive evidence of epilepsy; and a record taken during

the actual fit enables a differentiation to be made between hysteria and epilepsy. Abnormal electroencephalograms have been observed in a much higher proportion (60 per cent) of close relatives of epileptics than among normal controls (10 per cent). This suggests that an epileptic should not marry a person with an abnormal electroencephalogram, for fear of increasing the chance of hereditary transmission. Further points mentioned by the lecturer include the abnormal visceral auras which occur in many cases of major epilepsy. The most striking is the vasovagal attack which, unlike other forms of epilepsy, rarely occurs below the age of thirty; it may be associated with other epileptic manifestations and is characterized by extreme coldness combined with anginal symptoms. It may be due to an epileptic discharge arising in the medullary centres. Traumatic epilepsy is a not uncommon sequel of head injuries, especially when the dura mater has been opened. The aetiology is still unknown; possibly an hereditary cerebral dysrhythmia is the determining factor. Operation appears to benefit about half the patients thus treated.

F. Golla and W. G. Walter outline the technique and applications of electroencephalography. Records of differences of potential at several different points on the scalp are made with the help of a valve amplifier. In the normal brain rhythmic oscillations with a frequency of about ten per second are obtained from the occipital lobes when the subject's eyes are closed and his mind is at rest, that is during physiological inactivity. In various pathological conditions larger, slower and more irregular oscillations, the δ waves, occur. In connexion with organic cerebral lesions these waves indicate that nerve cells are in process of dying, and the degree of abnormality observed varies with the rate of cell destruction. Similar waves occur in about 50 per cent of epileptics, in an almost equal percentage of their healthy relatives and in at least 5 per cent of non-epileptic persons; they indicate a genetic abnormality which may eventuate in epilepsy. More than half the cases of behaviour disorder in children yield a similar result. Electroencephalography assists the physician both to diagnose epilepsy and to advise as to marriage and childbearing. In cases of head injury electroencephalography may prove to be of value as a means of predicting which patients are likely to develop fits in the future.

Diagnostic test

Positive water balance test for epileptic convulsions.—In most cases of suspected epilepsy diagnosis is not an urgent matter, but occasionally an early verdict is desirable. For such cases W. Blyth recommends a method of investigation depending upon the fact that retention of water in the body will precipitate a fit in a predisposed individual but will leave normal people unaffected. The test is simple; it occupies little time (the average being seventy-two hours) and, from subsequent observation of eighty-seven patients, it appears to give an accurate result in 86.6 per cent. Positive evidence that idiopathic epilepsy is present is given by the occurrence of a seizure, which may be of major or minor type. Failure to produce a seizure is not proof of the absence of epilepsy and in doubtful cases the test may have to be repeated. A positive water balance can be established merely by drinking large quantities of fluid but this method is disagreeable to the patient and takes a considerable time. More rapid results are obtained by the addition of intramuscular injections of pitressin (the pressor principle of posterior pituitary extract), which is an antidiuretic. Pitressin, owing to its other properties, is contra-indicated in diabetes mellitus, nephritis, arteriosclerosis and myocarditis, and these conditions should be excluded by routine examination before the test is performed. The routine method recommended is as follows. The patient is confined to bed throughout the test. An enema is given, he is made to pass urine and is then weighed. An ordinary diet is given, with copious fluids. The intake and output of fluid are measured and are charted daily, and the patient is weighed morning and evening. An increase of 2 per cent in the body weight with excess of intake over output is taken as proof that a positive water balance has been established. This point is usually reached in forty-eight hours. Pitressin, 0.25 cubic centimetre, is then given intramuscularly with 300 cubic centimetres of water by mouth. Further doses of pitressin, 0.5 cubic centimetre, with 300 cubic centimetres of water are given every two hours to a total of ten injections, unless a fit occurs before, when the test is stopped. Pallor, slowing of the pulse and a tendency to diarrhoea were noted but in no case were they severe enough to warrant the termination of the experiment. The combination of a positive water balance and administration of pitressin appeared to be necessary to precipitate a fit. It was found that neither did so alone.

Idiopathic and symptomatic epilepsy

Seizure patterns and voltage changes.—The comparative localizing values in epilepsy of clinical examination, of electroencephalography and of pneumoencephalography are discussed by H. Sjaardema and M. A. Glaser. The material studied consisted of fifty-two patients of whom twenty-four were classified as idiopathic epileptics: eighteen of them had seizure patterns. Of twenty-eight patients with symptomatic epilepsy fourteen had seizure patterns. In all, thirty-two patients showed seizure patterns, including thirteen with *grand mal* patterns, nineteen with psychomotor waves, seven with *petit mal* patterns and four with six-cycle waves. In sixteen patients hyperventilation was employed in an attempt, successful in twelve, to induce these convulsive patterns. Other abnormalities which occurred were increased β voltage in thirteen cases, unequal α voltage in sixteen, δ patterns in thirty-one and increased β voltage with δ pattern in twelve. In only two cases, both traumatic, was the electroencephalogram perfectly normal. In thirty-three patients (63.3 per cent) δ and seizure waves originated

in a circumscribed area of the brain. From a clinical point of view thirty-one patients (59.6 per cent) had focal epilepsy. The pneumoencephalogram was normal in eight cases; in the remainder (84.6 per cent) it showed some abnormality. The abnormalities included: unequal ventricles in thirty-five patients, decreased cortical air in eighteen, hydrocephalus in eleven, increased cortical air in eleven, ventricular shift in nine, subdural air in two, dilated third ventricle in two and a very small ventricle in one patient. In ten of the thirty-one cases of clinical focal epilepsy the electroencephalogram and the clinical signs localized the lesion in the same lobe. In nine others the two agreed as to side but not as to the lobe involved; in two of these nine cases the pneumoencephalogram and the clinical signs accurately localized the lesion. The pneumoencephalogram is often valuable in distinguishing between an organic lesion and idiopathic epilepsy.

Treatment

Drugs

Pyridine and hepato-renal disease.—L. J. Pollock, I. Finkelman and A. J. Arieff report two cases of hepato-renal disease in men aged thirty-two (fatal) and thirty-five years (recovery) to whom pyridine was given for epilepsy. Other epileptic patients were given smaller doses of pyridine (6 to 10 cubic centimetres rather than larger doses) without bad effects. The patient in the non-fatal case was regarded as having an astrocytoma of the left parieto-occipital lobe and was successfully operated upon; in the fatal case a necropsy was refused. In spite of the relatively low toxicity of pyridine in animals, the conclusion is reached that pyridine may be added to the list of chemical poisons causing the hepato-renal syndrome.

Soluble phenytoin and phenobarbitone.—Soluble phenytoin (sodium diphenylhydantoinate) has been used in cases of epilepsy with considerable success, but failures have occurred and H. H. Merritt and C. Brenner have endeavoured to reduce their number by combining administration of the drug with phenobarbitone. The treatment was given to 137 epileptics, 100 of whom had been treated previously by soluble phenytoin given alone in doses of from 3 to 10½ grains (0.2 to 0.6 gramme) a day for periods varying from one week to three years, and who had failed to respond satisfactorily; of the 100 patients, thirteen showed considerable and twenty-one showed moderate improvement; sixty-six were not improved. None of the patients who had only *petit mal*, psychomotor or Jacksonian seizures showed any improvement. Of the thirty-seven patients who had not previously received soluble phenytoin, thirty-four showed some improvement. To obtain good results from the combined treatment full doses must be given, for example soluble phenytoin, from 3 to 10½ grains, and phenobarbitone, from ½ to 5½ grains a day (0.05 to 0.3 gramme).

Convulsion therapy

Encephalographic changes.—B. L. Pacella and S. F. Barrera record some observations on the electroencephalographic changes associated with convulsion therapy by electrically induced fits. The changes consist in the development of slow waves, occurring singly or in groups. The authors find that the degree of variation and its persistence are roughly correlated with the number of seizures. This 'paroxysmal cerebral dysrhythmia' is very similar to the pattern observed in many epileptics and also seen after leptazol-induced convulsions, and the probability is that it is due, not directly to the passage of the current, but to the cerebral changes brought about by the convulsion itself. The minimum voltage required to produce a seizure was found to be within the same range for epileptics and non-epileptics, so that evidence was not forthcoming to suggest a lower threshold of excitability in the former. In epileptics convulsive therapy appears to predispose to further spontaneous fits, and may convert a latent into a clinically manifest case.

Preventive

Use of the electroencephalograph.—Under the name 'convulsive disorders', W. G. Lennox (1943¹) discusses the prevention and treatment of epilepsy known under twenty-seven titles, such as 'the sacred disease', 'morbus committalis', the 'falling sickness', 'fits' and recently 'paroxysmal convulsive disorders', the choice of the American Neurological Association. Traditionally the aetiological factors of epilepsy have been separated into two groups: (1) 'idiopathic', 'cryptogenic', 'constitutional', or 'hereditary', which Lennox prefers to call 'genetic', and (2) 'symptomatic', the result of some pathological condition, and termed by Lennox 'acquired'. From a study of many thousands of articles during twenty years Lennox found very few on the important subject of prevention; he states that three-fourths of epilepsies are of a genetic origin, and one-fourth due to one or more of the environmental factors. The prevention of epilepsy is now more feasible than formerly and this is due to new knowledge provided by electroencephalography, of which Lennox with F. A. and E. L. Gibbs made and classified observations on 1,000 normal control persons, on 1,260 epileptics, 320 near relatives of epileptics, and eighty twins (160 co-twins). The principal methods of preventing epilepsies are as follows. (1) Prevention of cerebral dysrhythmia rather than of epilepsy, by eugenics; (2) prevention of acquired conditions which act as a precipitant of seizures; and possibly the treatment of persons who have either hereditary or acquired dysrhythmia in the pre-seizure period. The important aspects of treatment are removal of acquired causes, improvement of general physique, the use of anti-convulsants, especially soluble phenytoin, and efforts to strengthen the psychological and social position of the patient. War increases both the relative and absolute numbers of epileptics, and makes it harder for those rejected for the services to secure employment.

EDITORIAL COMMENTARY—Main Factors in Epilepsy Investigation

Much work continues to be done on electroencephalography in epilepsy, but recently writers have stressed the complexity of the subject and the difficulty of correlating clinical and electroencephalographic data. Thus K. H. Finley and J. B. Dynes (1942) studied the electroencephalogram in 626 unselected epileptics. The five clinical types of epileptic disturbance were (1) *grand mal*, (2) *petit mal*, (3) mixed *grand mal* and *petit mal*, (4) Jacksonian and (5) psychomotor. The authors did not find a characteristic electroencephalogram for any of these clinical types. Of the 626 epileptics 14 per cent had a normal electroencephalogram, and 86 per cent had a borderline or abnormal electroencephalogram. The abnormal records fell into eighteen groups, none of which contained more than 10 per cent of the total number of subjects. The present significance of electroencephalography in the diagnosis of epilepsy is as follows. (1) From 10 to 20 per cent of epileptics have a normal electroencephalogram and the percentage is higher in those having *grand mal* only. A normal electroencephalogram therefore does not exclude epilepsy. (2) Patients with *petit mal* usually exhibit the wave-and-spike pattern or a 3 per second wave, but the abnormal rhythm may be present only after overventilation. (3) These rhythms, however, are not pathognomonic of *petit mal* but may occur in other forms of epilepsy. (4) *Grand mal* is not associated with any characteristic electroencephalogram, but diffuse multiple spikes with rapid rhythms are usually associated with *grand mal* (H. Jasper and J. Kershman, 1941). (5) Focal epileptogenic cortical lesions are often associated with corresponding focal abnormal electroencephalographic discharges. (6) There is no abnormal electroencephalogram which is pathognomonic of epilepsy. Cortical dysrhythmia may express itself as epilepsy, psychoneurosis, psychosis or psychopathy (D. Williams, 1941). (7) An abnormal electroencephalogram can therefore only be interpreted in relation to the clinical history of the patient. An abnormal electroencephalogram has been accepted in a court of law as evidence that a man accused of murder committed the crime as a result of an attack of epilepsy.

The great concentration of interest during recent years upon the electrical cortical changes in epilepsy has rather distracted attention from other factors which may be no less important. It is many years since Fay claimed that prolonged restriction of water intake was beneficial in epilepsy. Stone, Arieff and Lohan (1942) found that the ingestion of 2,000 cubic centimetres of water in fifteen to thirty minutes by epileptic patients hardly reduced the specific gravity of the blood. W. Blyth (1943), however, obtained a positive water balance by giving large quantities of fluid for forty-eight hours or longer, and then increased hydration by a series of pitressin (the pressor factor of posterior pituitary extract) injections, and he was able to precipitate convulsions in 86.6 per cent of suspected epileptics. This test may be of diagnostic value. Stone, Arieff and Lohan's observations render it unlikely that in the epileptics the water metabolism as such is disordered: probably their susceptibility to hydration is due to its effect upon the permeability of their nerve cells.

There has now been time to assess the value of soluble phenytoin (sodium diphenylhydantoinate, dilantin sodium, epanutin). G. M. Tullidge and J. T. Fox (1942) report that, out of forty-three patients who had taken the maximum dose, twenty-four were completely freed from fits and sixteen were almost completely freed, but 'with the effective therapeutic dose grave toxic signs calling for withdrawal will occur in at least a third of the cases'. Patients with major fits and psychomotor attacks respond well; those with *petit mal* rarely respond. In the routine treatment of epileptics it is best to begin with phenobarbitone, and, only if this fails, to give sodium diphenylhydantoinate. A combination of the two drugs may be more effective than either alone (see above). The value of bromide should not be forgotten, and prominal (phemitone) is also a useful drug. Benzedrine sulphate in doses of from 5 to 7½ milligrams enables the dose of phenobarbitone to be substantially increased without causing depression. The most recently published figures of the results of the late surgical treatment of traumatic epilepsy are those of W. Penfield and T. C. Erickson (1941). Sixty-two patients with a meningo-cerebral cicatrix were treated by excision: 22.5 per cent were freed from attacks and the same number were almost completely freed. A further 32 per cent were considered to be 50 per cent improved.—W. RUSSELL BRAIN

Arieff, A. J., and Yacorzynski, G. K. (1942) *J. nerv. ment. Dis.*, **96**, 49.

Barbour, H. G., and Hamilton, W. F. (1926) *J. biol. Chem.*, **69**, 625.

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Golla, F., and Walter, W. G. (1943) *Practitioner*, **150**, 165.

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— (1943) *Ann. intern. Med.*, **18**, 145.

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Pacella, B. L., and Barrera, S. E. (1942) *J. nerv. ment. Dis.*, **96**, 125.

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Pollock, L. J., Finkelman, I., and Arieff, A. J. (1943) *Arch. intern. Med.*, **71**, 95.

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- Stone, T. T., Arieff, A. J., and Luhan, J. A. (1942) *Arch. Neurol. Psychiat., Chicago*, **48**, 407.
 Tullidge, G. M., and Fox, J. T. (1942) *Lancet*, **2**, 6.
 Williams, D. (1941) *J. Neurol. Psychiat. N.S.*, **4**, 257.

EPILOIA

See also B.E.M.P., Vol. V, p. 117.

Morbid anatomy

Nature of epiloia

Melorheostosis.—G. S. Hall, who described in 1940 the clinical features of a case, now gives a full account of it under the title of melorheostosis. Unusual bone changes associated with tuberous sclerosis occurred in a boy, aged seventeen years, of subnormal mentality and with characteristic facial adenoma sebaceum. Death was the result of fits and of other symptoms due to raised intracranial pressure caused by tuberous sclerosis. The patient had been under the author's personal care for four and a half years and had been the subject of this rare chronic affection for twelve years before death. With regard to the necropsy report, the bone lesions in the radial half of the right hand are described as showing two outstanding features, namely prolific intramembranous ossification of immature character and absence of the periosteum, both of which are due to a local disorder of osteogenesis. The characteristic lesions of tuberous sclerosis were present in the brain, eyes and kidneys. It is suggested that the association of melorheostosis and tuberous sclerosis may be an expression of a mesodermal defect of unusual distribution and form. The defect may involve any part of the skeleton in which membrane bone is formed, although essentially it is a disturbance of ossification in connexion with diaphysal bone, that is bone originally laid down in cartilage.

Hall, G. S. (1940) *Quart. J. Med. N.S.*, **9**, 10.

— (1943) *ibid.*, **12**, 77

ERYTHRAEMIA

See also B E M P, Vol V, p 176; and Cumulative Supplement, Key No 443

Clinical picture

Blood pressure

W S Tinney, B. E. Hall and H. Z. Giffin refer to previous observations made at the Mayo Clinic showing that among 163 cases of erythraemia there were ten (or 6 per cent) cases of coronary occlusion, in four of which angina pectoris also existed. Sixty-five patients (or about 40 per cent) of the 163 cases of erythraemia had a systolic blood pressure above 150 millimetres Hg and in fifteen (or 9 per cent) above 180 millimetres Hg. The fact that patients with erythraemia may have multiple vascular lesions was well illustrated by two patients who had lesions in the peripheral, cerebral and coronary arteries.

Hepatic and splenic complications

Importance of leukaemoid reaction.—W. S. Tinney, B. E. Hall and H. Z. Giffin review the condition of the liver and spleen in erythraemia. They found that some hepatic complication was shown by forty, or 25 per cent, of 163 cases of erythraemia: in thirty-one cases the liver was palpable halfway to the umbilicus. A definite clinical diagnosis of hepatic cirrhosis was made in five cases, and in three of the five cases severe and repeated haemorrhagic manifestations occurred usually in the form of purpura, haematuria, or after minor operations; two of the patients with evidence of liver damage had gout. Ascites was present in six cases, and a clinical diagnosis of portal thrombosis was made in six cases, but was proved at necropsy in two only. Severe jaundice supervened in three patients before treatment by phenylhydrazine. The spleen was easily palpable in 107, or 66 per cent, of the 163 cases, in seventeen of these cases the spleen reached the umbilicus. A clinical diagnosis of splenic infarct or of perinephritis was made in eleven cases, in nine before treatment with phenylhydrazine and in two after that form of treatment. In two cases the spleen was so large and painful that splenectomy for symptomatic relief was considered. In fifteen cases, in which the spleen was greatly enlarged, a leukaemoid reaction was present; in five of these the leukaemoid reaction was so extreme that the blood smears closely resembled those of myeloid leukaemia; four of these five patients lived for long periods, twelve, fifteen, twenty and twenty-three years respectively after the diagnosis of erythraemia was made. In seven cases of very large spleen the leukaemoid reaction was absent. It is pointed out that although the degree of splenomegaly and the presence of a leukaemoid reaction seem to be directly correlated with the duration of the disease, this was not always true.

Complications

Intracranial tumour and hypertension.—G. E. Carpenter, F. Walker and H. Schwartz describe two cases which showed erythrocyte counts of seven and eight millions; one patient was a hypertensive. From both the patients intracranial tumours (cerebellar haemangioblastomas) were removed and the polycythaemia passed off in each case; the hypertension also abated in the second case.

Carpenter, G. E., Walker, E., and Schwartz, H. (1942) *Proc. Inst. Med., Chicago*, **12**, 182.

Tinney, W. S., Hall, B. E., and Giffin, H. Z. (1943) *Proc. Mayo Clin.*, **18**, 46.

— — — (1943) *ibid.*, **18**, 94.

EYE EXAMINATION

See also B.E.M.P., Vol. V, p. 216.

Instruments and technique of using them*The ophthalmoscope*

Ophthalmoscopy in clinical medicine.—An address given by A. M. Ramsay to the Bute Medical Society deals with ophthalmoscopy in clinical medicine. The fundus oculi affords an unique opportunity for the study of vital processes, and the routine use of the ophthalmoscope may enable the general practitioner to detect disturbances of health in their earliest stages. One of the earliest signs of pathological high blood pressure is constriction of some of the branches of the retinal artery. Straightening of the course of the vessel may be associated with constriction and is usually evidence of organic disease. Fully developed arteriosclerosis is visible in the retinal arteries, which appear irregularly contracted and abnormally tortuous and show a characteristic brightness of the central light streak. Where an artery crosses a vein the latter is concealed from view. Haemorrhages may be seen in the retina even before symptoms occur. Retinitis is a frequent concomitant of arteriosclerosis, nephritis and diabetes.

Routine examination*Fundus*

Dangers of atropine.—J. E. Martin comments upon the risk of precipitating glaucoma by the use of atropine. The effect of atropine on the intraocular muscles cannot be reversed by eserine and several days may elapse before it wears off. With advancing age the lens enlarges and pushes the iris forwards, reducing the narrow drainage angle between the iris and the cornea, especially when the cornea is comparatively small. Age is not a contra-indication to atropine unless drainage is thus impaired. If the intra-ocular pressure is at all raised, homatropine, the action of which is reversible by eserine, should be used when mydriasis is required.

Martin, J. E. (1943) *Brit. med. J.*, **1**, 631

Ramsay, A. M. (1943) *Brit. med. J.*, **1**, 685.

EYELIDS, INJURIES AND DISEASES

See also B.E.M.P., Vol. V, p. 239.

Inflammation*Treatment*

Dermatological applications.—A. Linksz shows how the principles of dermatological treatment may be applied to the especially delicate skin of the eyelids. (1) Washing and cleansing. Water, preferably softened with sodium borate or camomile, is useful in seborrhoeic blepharitis. In impetigo boric lotion may be substituted. Water should be avoided in dry eczema or in any acute dermatitis of the lids, in the later stages of herpes and when fissures (rhagades) are present. In these cases cleansing should be done with pledgets of cotton-wool soaked in olive oil, castor oil, liquid petrolatum or, best of all, cod-liver oil. In chronic seborrhoeic blepharitis a toothpick swab dipped in benzene, tincture of iodine, hydrogen peroxide or silver nitrate solution is useful; oily preparations should be avoided unless sepsis is present or very adherent crusts have formed. Water has a drying effect on the skin. (2) Hot and cold applications. For application to the skin solutions of slightly acid reaction (for example boric acid) are better than plain water. In the aged and in persons with dry skin cold cream or oil should be applied before hot compresses are used. (3) Cold creams. These have a prolonged lubricating and cooling effect and are especially useful for dry skin. (4) Pastes, which consist of a mixture of powder and fat and therefore adsorb secretions, can be applied to weeping lesions for which either ingredient alone would be harmful. They are particularly useful in cases of maceration of the skin resulting from epiphora. Preliminary formation of an eschar by the use of 5 per cent silver nitrate solution is useful. Pastes are less irritating than ointments and are therefore suitable for acute lesions. Refrigerating pastes containing a fat with hygroscopic properties possess the qualities both of a cold cream and of a paste, and are useful in eczema. (5) Ointments are useful in blepharitis after thorough cleansing and removal of scabs. The incorporation of a non-irritant base is important. (6) Counterirritants. Tincture of iodine is helpful in seborrhoeic blepharitis. The author also deals with the effects of dyes used cosmetically and emphasizes the need for caution, especially with the heavy metals, but states that harmful effects of such dyes are very rare in comparison with their widespread use.

Linksz, A. (1942) *Arch. Ophthalm., N.Y.*, **28**, 959.

FIBROSITIS

See also B.E.M.P., Vol. V, p. 279; and Cumulative Supplement, Key No. 489.

Treatment*Physical methods*

The painful shoulder.—Under this title R. J. W. Withers describes a well-defined clinical group of cases characterized by pain, limitation of movement and muscular wasting, not due to tuberculosis, infective arthritis, fractures, dislocations and tumours of bone. So-called minor injuries and affections of the shoulder, often described as 'neuritis' or 'rheumatism',

form an important part of orthopaedic practice. The lesion has also been given the labels bursitis, tendinitis, periarthrititis, arthritis, synovitis and capsulitis, the last three of which are not applicable. The author has had experience of nearly 200 cases and concludes that most are due to an underlying inflammation of tendons, which may be traumatic, irritative or adhesive. Treatment consists of (1) stretching adhesions, either gradually or suddenly, and (2) building up of the atrophied muscles by exercises, stress being laid on the value of activity on the patient's own part. It is doubtful if massage and diathermy are of very much value. Gradual stretching of adhesions can be carried out by putting the patient to bed without pillows and by tying the wrist of the affected arm to the top of the bed. The head end of the bed is then gradually blocked up so that the patient tends to slide downwards in the bed; the result of this manoeuvre is that the arm takes up a position of abduction and external rotation. The method is excellent, but unfortunately causes a considerable amount of pain, so that the patient must be kept under morphine. Sudden stretching is effected by manipulation with the greatest gentleness under general anaesthesia, and several manipulations may be needed.

Withers, R. J. W. (1942) *Ulster med. J.*, **11**, 1.

FILARIASIS

See also B.E.M.P., Vol. V, p. 301; and Cumulative Supplement, Key Nos. 490–495.

Definition and classification

Distribution of various forms

Filariasis in East Africa.—F. Hawking reviews the literature relating to filariasis in East Africa. He finds that *Wuchereria bancrofti* is common in most districts. In the Zanzibar Protectorate the microfilarial rate in adults averages 33·36 per cent, in Tanganyika 17·64, in Kenya 18·4. *Acanthocheilonema perstans* is common in the regions north, west and south-west of Lake Victoria and in the Liwale district; in Uganda the microfilarial rate averages 28·05 per cent. *Loa loa* is almost unknown. *Onchocerca volvulus* occurs in limited areas. *Dracunculus medinensis* only in northern Uganda, where it appears to be endemic; in 1934, 2,028 cases were treated in the whole territory.

Filariinae

Wuchereria bancrofti

Infestation of the eye.—A case of infestation of the eye by a nematode is recorded by B. de Meillon and J. C. Gillespie. The patient, a woman, had travelled in Central Africa for some years. In 1937 she developed urticaria which has recurred at intervals ever since but it has been milder since the removal of the worm. In 1942 two swellings appeared in the forearm and after they had subsided the face swelled and a worm was seen in the subconjunctival tissue above the lower fornix of the right eye. The worm was removed under cocaine anaesthesia through an incision in the lower fornix. It was of the family *Filariidae*, and was about four inches long.

Hawking, F (1943) *J. trop. Med. (Hyg.)*, **45**, 159.

de Meillon, B., and Gillespie, J. C. (1943) *S. Afr. med. J.*, **17**, 5.

FOETUS DISEASES. MALFORMATIONS AND MONSTROSITIES

See also B.E.M.P., Vol. V, p. 334; and Cumulative Supplement, Key Nos. 503–512.

Abnormal conditions occurring in living foetus

Skeleton

Craniofacial radiological diagnosis.—J. B. Hartley and C. W. F. Burnett have collected twenty-eight cases of a rarely recognized developmental anomaly of the vault bones of the foetal skull, the bones at the base of the skull being normal. They show that cases are less rare than is thought, and give the reasons why. The condition is usually associated with other congenital defects such as spina bifida, encephalocele, hydrocephalus, craniosynostosis or talipes. It occurs in two main forms. The less advanced is characterized by depressions on the inner surfaces of the vault bones—for this form the name, craniofacial, should be retained; in the more severe form, for which the name craniofacial is suggested, there are areas of actual absence of bone. Radiological examination may show the presence of the defect during foetal life, at the time of birth or later. The presence of hydramnios, hydrocephalus or a maternal history of still-births indicates the advisability of a radiological examination. The authors show that the defect is quite common, and that it is often associated with conditions likely to cause still-birth. The presence of craniofacial predisposes to death in early infancy and makes the outlook worse in infants with meningocele. In the rare cases in which craniofacial occurs alone it is probable that the infant will live and that the lacunar changes will gradually fade as the bones of the skull develop; when hydrocephalus is also present the prognosis is not good, quite apart from the possibility that perforation of the foetal skull may be necessary to effect delivery. The presence of craniofacial should be regarded as being in itself of little danger; its importance is that its recognition in an antenatal radiograph suggests the presence of some other more serious developmental abnormality.

Digestive system

Congenital atresia of the duodenum.—L. M. Wiig and O. T. Claggett review the subject of

congenital atresia of the duodenum. The condition may be either (1) extrinsic, caused by peritoneal bands or adhesions, or (2) intrinsic. The latter type may be of three forms, namely (a) diaphragmatic, with obstruction just below the level of the biliary papilla; (b) duodenal, with part of the duodenum forming a cord-like structure of varying calibre which connects the two partially blind ends; (c) the most serious form, with complete division of the duodenum, prone to prove fatal if not successfully operated upon in the first twelve days of life. In one case of this kind an operation was successfully carried out on the twenty-fifth day of life; partial congenital atresia of the second or third part of the duodenum was present, but it could not be seen as it was retroperitoneal; there was not any evidence of intestinal obstruction. Posterior gastro-jejunostomy was performed.

Congenital intestinal obstruction in the new-born.—J. W. Duckett reports six cases of congenital obstruction of the intestine in the new-born. The condition should be suspected when persistent vomiting begins soon after birth. The presence of bile in the vomit, with the early onset, distinguishes the condition from congenital pyloric stenosis. Obstruction may be intrinsic, the commoner or extrinsic type resulting from abnormal peritoneal bands. X-ray examination is helpful in diagnosis, plain films usually provide sufficient evidence and barium administration is dangerous and should be avoided if possible. Without operation death quickly occurs; pre-operative infusion or transfusion may be required. Ether anaesthesia gives satisfactory relaxation for operation. Extremely gentle handling and complete haemostasis are essential. Primary anastomosis is the procedure of choice in intrinsic obstruction. Fine cotton (no. 100) is recommended as being the only suitable suture material. Post-operative transfusion, gastric suction and lavage are valuable. Of the six cases described by the author, one patient died before operation could be attempted, two died after operation and three, including the only one with extrinsic obstruction, recovered.

Respiratory system

Agenesis of the lung.—V. O. B. Gartside reports a case in a healthy boy, aged seven years, and reviews the subject of agenesis of the lung, of which S. Hurwitz and H. B. Stephens in 1937 collected thirty-five cases and pointed out the occurrence of associated abnormalities, such as anal stricture, absence of the diaphragm, oesophago-tracheal fistula, accessory thymus and hypoplasia of the face. Necropsies have shown two separate conditions. In one the bronchus ends in a blind sac without any suggestion of lung tissue on that side; in the other form there is a rudiment of lung tissue which may or may not have been created during life. The pleura may be absent or present. In Gartside's case there were bilateral cervical ribs, spina bifida, wedge-shaped vertebrae, fusion of ribs, congenital high scapula and a congenital heart lesion, probably a septal defect. The condition cannot be recognized by ordinary clinical examination and depends on radiograms and a bronchogram. It is a primary condition due to an error of development in the germ plasm. Of thirty-three cases in which the sex was known nineteen were males. Absence of the left lung occurred in twenty-three out of thirty-seven cases. Radiograms show opacity on the affected side with displacement of the trachea and mediastinum. Of the published cases three were still-births, six patients died in less than a week, thirteen died in less than six months. In cases with oesophago-tracheal fistula food passes into the lungs and causes rapidly fatal pneumonia.

Genito-urinary system

Congenital absence of vagina.—W. S. Whittemore reports a case of operation for congenital absence of the vagina in which the patient, whom the fortunate chance of a congenital cervico-vesical fistula saved from developing a haematometra, subsequently became pregnant. She entered hospital, at the age of twenty-one, complaining of attacks of pain which had occurred every two months since the age of sixteen and which for the eighteen months prior to admission had been associated with slight urethral bleeding on micturition. She had never menstruated and, since marriage three years before, had never had successful marital relations. On examination the vaginal orifice was absent and a finger which was introduced into the rectum could feel nothing between the rectal wall and the urethra. The uterus was felt to be shaped normally. Cystoscopy revealed absence of the left ureteric orifice. No abnormal opening into the bladder could be seen. Intravenous pyelography did not show any left pelvic shadow. A plastic operation to construct an artificial vagina was performed, the new tube being lined with pedicled flaps which were taken partly from the skin and partly from the mucous membrane of the labia minora. In the course of the operation a fistulous track was found which connected the cervical canal with the bladder. After healing, dilatation was performed regularly twice a week for six months. Conception took place about three months after operation and at full term the patient was delivered by Caesarian section of a normal child. The uterus was of the unicornate type, with absence of the left adnexa. Two years after the operation the patient became pregnant for a second time.

Duckett, J. W. (1942) *Ann. Surg.*, **116**, 321.

Gartside, V. O. B. (1943) *Brit. J. Radiol.*, **16**, 69.

Hartley, J. B., and Burnett, C. W. F. (1943) *Brit. J. Radiol.*, **16**, 99.

Hurwitz, S., and Stephens, H. B. (1937) *Amer. J. med. Soc.*, **193**, 81.

Whittemore, W. S. (1942) *Amer. J. Obstet. Gynec.*, **44**, 516.

Wiig, L. M., and Clagett, O. T. (1942) *Proc. Mayo Clin.*, **17**, 577.

FOOD

See also B.E.M.P., Vol. V, p. 388; and Cumulative Supplement, Key Nos. 513–518.

Calorific value of food*Calories*

National bread and wholemeal bread values.—N. C. Wright compares the digestibility of national wheatmeal with that of straight-run white flour. He criticizes results obtained by H. A. Krebs and K. Mellanby on the ground that the wheatmeal used by them contained less fibre than the standard national wheatmeal, and that digestibility depends upon the amount of fibre. Comparing the results obtained by other workers, he finds that in all cases digestibility falls with increasing extraction. The following mean values are arrived at: protein digestibility of white flour, 86 per cent; of national wheatmeal, 81 per cent; energy digestibility of white flour, 92 per cent, of national wheatmeal, 88 per cent. The actual protein and energy contents are as follows: protein—white flour, 12.00 per cent, national wheatmeal, 12.35 per cent; caloric value of both flours 364 per gramme. From these figures it is calculated that over 60,000 tons of protein and 1,600,000 million calories are wasted yearly as a result of the adoption of the national loaf, and that such losses would be more than doubled if the wholemeal loaf were adopted.

Food requirements and intakes*Minimum and optimum requirements*

Inorganic elements.—In the first of the Harben lectures for 1941 E. V. McCollum discusses the nutritional problems presented by certain inorganic elements. (1) Calcium and phosphorus. The daily human requirement of calcium has been estimated, on the basis of calcium loss, as being from 0.45 to 0.65 gramme for adults, and as about 0.8 gramme for children of from six months to two years of age, increasing with growth to 2 grammes for adolescents. Pregnant women require from 1.5 to 3 grammes. The metabolic requirement of phosphorus is about 25 per cent greater than that of calcium. Many of the poorer American families have been found to be living on diets deficient in the above two elements. Senile osteoporosis may be a result of chronic deficiency. Absorption of calcium from vegetable foods is incomplete, and the only good sources of calcium are milk and cheese. Vitamins A and D are essential for calcium metabolism. (2) Iron. To be absorbable, iron must be soluble, ionizable, in the ferrous state and ultrafiltrable. Small amounts of copper and of vitamin C are necessary for its utilization; very little (about 6.5 milligrams daily) is needed normally, because it is used over and over again, but growing children and pregnant women need more. (3) Iodine. The incidence of endemic goitre in Michigan has been reduced almost to nil since iodized salt was introduced. Vitamin K appears to play a part in iodine metabolism; if animals fed on a diet free from vitamin K are given sulphaguanidine, which prevents synthesis of this vitamin in the intestine, they develop thyroid hyperplasia. If the result were the same in human subjects, it would be a serious drawback to the therapeutic use of sulphaguanidine.

Nutrition of industrial workers.—The quality of the meals taken by the industrial worker is important in relation to his health and morale. R. Goodhart has examined the nutritional condition of about 1,000 workers and found that in 42 per cent the ascorbic acid level of the blood was below 0.5 milligram per 100 cubic centimetres, 47 per cent showed evidence of gross vitamin A deficiency and 19 per cent had signs of premature degeneration of the nervous system. The writer also inspected the lunches chosen by workers from the canteens and nearly always found that at least 50 per cent of the workers selected poorly balanced meals, even when a good choice was available. These findings were confirmed by other investigators. Few of the workers took a green vegetable or salad, and practically none ate wholemeal bread. The cost of a balanced meal is an important consideration, and the remedy suggested is that canteens should serve a standard cheap lunch which satisfies the worker's nutritional requirements.

Goodhart, R. (1943) *J. Amer. med. Ass.*, **121**, 93.

Krebs, H. A., and Mellanby, K. (1942) *Lancet*, **1**, 319.

McCollum, E. V. (1942) *J. R. Inst. publ. Hlth Hyg.*, **5**, 165.

Wright, N. C. (1942) *Lancet*, **2**, 165.

FOOD POISONING

See also B.E.M.P., Vol. V, p. 401.

Clinical picture*Salmonella septicaemia*

Typhoid character of reaction.—*Salmonella (Bacillus aertrycke)* septicaemia is a rare form of salmonella infection of which seven cases were observed by J. Keeling at Auckland Hospital. The patients came from widely scattered localities, and in only one instance could contact be established with the source of infection. The patients' ages ranged from thirteen years to sixty-four years. The onset was acute in five cases. In one case staphylococcal septicaemia was also present, and the patient concerned and one other died. Blood culture in all cases yielded a Gram negative motile bacillus giving negative fermentation reactions in lactose and saccharose and positive reactions in dextrose and mannite. By means of agglutination reactions and absorption technique, the organism was finally identified as *B. aertrycke*. Not in a single case

did the serum agglutinate the organism isolated from the blood. The illness was of a typhoid character. Jaundice was a prominent feature in two cases. Localization occurred in one case in the meninges and in another in the lungs. In the former the connexion between the meningitis and the salmonella septicaemia was therefore not directly proved, but it was inferred from the fact that the cerebrospinal fluid was sterile on culture and contained a very high proportion of lymphocytes, contrary to the usual findings in meningococcal infection. Keeling, J. (1942) *N.Z. med. J.*, **41**, 254.

FOOT, DISEASES AND DEFORMITIES

See also B.E.M.P., Vol. V, p. 412.

Deformities

Acquired deformities

Foot pain in soldiers.—A Leading Article in the *Lancet* draws attention to the problem of foot pain in soldiers. Pain is the foot's main safeguard and, if ignored, the patient may develop malposture and recurrent foot strain. It may arise at three stages in a man's army life—on enlistment, at physical training and after route marching. Most of the trouble is due to the breaking down of apparently normal feet, and cases of men entering the Army with obvious foot defects are relatively uncommon. The adoption of the heavy army boot throws a temporary strain on the tibialis anterior muscle, which may lead to chronic fatigue or to acute tenosynovitis. The long extensor muscles of the toes are then used to dorsiflex the foot, so that corns or sore places develop on the toes from rubbing against the toecap, eventually, by simultaneous use of all the extensor muscles, a valgus foot with clawed toes is produced. During physical training a symptomless hallux rigidus may develop as the result of certain exercises done in Plimsolls. In route marching an acute foot strain with flattening of the metatarsal arch is apt to occur. The patient with a painful foot usually requires hospital treatment, which should include preliminary rest in bed.

Foot strain in war workers.—Painful feet in relation to war work is the subject of a symposium in the *Medical Press and Circular*. The pain of the weak foot, according to N. C. Lake, arises in the connective tissues, that is the ligaments and fasciae, and not in the muscles of the foot. The pathology of the process is unknown. It has been suggested that overstretching of non-contractile tissues may set up a vasomotor reflex resulting in a process of aseptic inflammation, associated with pain, tenderness and swelling. The softening caused by inflammatory changes would weaken the connective tissue structures and allow them to elongate. Difference of opinion exists whether the changes in the non-contractile tissues are primary or are secondary to the failure of the muscles which support and reinforce them. In cases of pure fatigue the foot is more or less normal after a night's rest, but as the day goes on pain, tenderness, weakness and a sense of heat develop, and the worker's thoughts may become so concentrated on his feet that his work suffers seriously. Work at a bench or machine usually involves a stance in which the weight of the body is taken not by the heel, as it should be, but further forward. The use of a metatarsal bar may give relief, and an inclined platform for the workers to stand on is suggested as being worthy of consideration. Workers could often sit at their bench; they should be educated in standing, however, and in the use of proper footwear with low heels and wide toes. A. T. Fripp recommends for chronic cases manipulation of the foot under anaesthesia in order to restore mobility, with subsequent muscular re-education. Patients with acute foot strain, which usually occurs in young adults, should be treated, after bone lesions have been excluded by X-ray examination, by complete rest at first and, when the pain has subsided, by physiotherapy. Spasmodic flat-foot is mostly seen in adolescents starting work which involves an unwonted amount of standing; it originates in spasm of the peroneal muscles. Treatment consists in immobilization in plaster. If possible the valgus deformity is first overcome by manipulation under anaesthesia but, if this is impossible, the plaster must be applied to the foot in the valgus position. The plaster is worn for from four to six weeks and during this time a walking apparatus is made, consisting of an outside iron and inside T-strap. This is worn with a felt and leather arch support for a further period. The patient's occupation must be changed for a more sedentary one. Patients with march fracture should be treated in plaster and later by physiotherapy. For sprains of the foot and ankle, early active movement is most important to prevent the formation of adhesions and to hasten recovery. For recurrent sprain the heel of the shoe should be buttressed (not thickened) on the outer side. For lacerations and compound fractures, treatment on general principles is given; the closed plaster cast is now the accepted method of immobilization. The importance of proper footwear was emphasized by H. Bradley, Director of Research, the British Boot, Shoe and Allied Trades Research Association.

Defects in children

Congenital flat-foot: its diagnosis and treatment.—J. G. Kuhns discusses the 0.5 per cent of children whose feet fail to develop satisfactorily and continue to show ligamentous relaxation with displacement of the medial tarsal bones inwards and downwards on weight bearing. Hereditary factors appear to play a part in the causation of this congenital flat-foot which, if untreated, leads to much disability in adult life. In babies the diagnosis is made by observing the abnormal suppleness of the foot, of which the dorsum can often be made to touch the tibia. In children who are able to stand, extreme valgus is found, with inward and downward

displacement of the astragalus and scaphoid. The child shows defective balance and great awkwardness; walking is delayed and the shoes soon become misshapen. After the age of six deformities of the bones and subluxations often develop; in the second decade arthritis may occur. Symptoms depend upon the severity of the strain. Lasting relief is rare if treatment is not begun during the first decade of life; it should be started as soon as the diagnosis is made and should be continued without interruption until the foot is able to bear weight in a normal position. Proper feeding, rest and exercise are of great importance. The most effective local treatment in infancy is some form of support, such as a bivalved plaster cast, to hold the foot in inversion and plantar flexion. When the child begins to stand he is fitted with a short caliper brace and instep pad or, in severe cases, an attached foot-piece. Exercises are begun as soon as the child is old enough. In cases not seen early, relief of symptoms can usually be secured by means of proper shoes with supports under the arch and under the inner side of the heel. For severe disability in patients over twelve years of age, operation may be required.

Painful conditions

Treatment

Army cases.—In a Discussion on painful feet, C. Lambrinudi stated that in his experience of Army cases one-third of the orthopaedic patients complain of foot troubles. The problem is primarily one of muscular fatigue; footwear is a factor of secondary degree. Training is of the first importance. Even feet with some structural abnormality can be gradually worked up to a surprising pitch of efficiency. The balancing test is the best index of the capabilities of the borderline foot, because good balance implies good muscular tone. Patients with valgus foot should not be treated by inside wedges, because supports and training are incompatible terms. The foot should be rested until all pain disappears, after which tone is restored by balancing exercises, at first without and later with outside wedges to add to the load on the muscles. The supinated foot should be graded down and fitted with an arch support. The foot with slight cavus makes standing very difficult. Pain in the flexor brevis muscle causes the patient to walk with the toes cocked or in the claw position. If each toe is flexed separately against resistance one or two painful toes can usually be found, and pressure along the line of these gives rise to acute pain, abolished by injection of novocain (procaine hydrochloride) at the tender spot. E. J. Crisp pointed out that feet can be divided into three types, the ultra-broad (ratio $2\frac{1}{2}$ to 1), the ultra-narrow (3 to 1 or over) and the average ($2\frac{1}{2}$ to 1). Patients with the first two types respond very badly to treatment; those with the third type almost invariably recover completely. A short tendo Achillis is a serious defect in a soldier; dorsiflexion to 10° or 15° is essential for proper function. Men with this deformity should be rested in hospital until the foot recovers and should then be regraded to category B7; the high longitudinal arch is also an indication for this category. The ultra-broad foot is deficient in spring, mobility and coordination, and is an indication for rest and exercises with subsequent regrading. The ultra-narrow foot is associated with poor general physique and tone and also indicates regrading. H. L.-C. Wood had found the results of manipulation on the whole disappointing. He pointed out that patients are rarely seen early enough. W. R. Bristow urged upon regimental medical officers the importance of recognizing early stages of foot strain. W. H. Gervis emphasized the importance of securing adequate intrinsic function by physiotherapy and by proper footwear.

In civil practice.—J. J. Nutt discusses the subject of painful feet from the point of view of the general practitioner. In the diagnosis of painful conditions of the foot, a careful taking of the history is the first essential. If the feet were painless until recently, does the trouble date from a change in the style of footwear or in the patient's daily routine? Are the feet painful on rising or does the pain develop during the day? Examination shows the appearance of the foot and how the patient uses it, and demonstrates any tender spot. If it is found that the foot is used in the everted and abducted position, the diagnosis of 'weak foot' or 'pronated foot' can be made with confidence. If spasm of the peroneal muscles prevents full passive inversion and adduction, hot foot baths and absolute rest are ordered and, if after a few days free passive movements are not restored, an X-ray film should be taken to exclude any possibility of bone or joint disease. Treatment for the weak foot is directed to restoring the normal position and function. A wedge, from one-eighth to one-quarter inch in thickness, is placed on the antero-medial part of the heel of the shoe and a similar thicker wedge, flared medially, along the medial border of the instep of the shoe, filling the space between the first metatarsal bone and the ground. The shoe must be flexible. Adhesive strapping is used at first to help the weakened muscles. The patient must be taught to walk with the toes pointing straight forwards or, better, inwards. Exercises are inferior to any kind of sport such as dancing which keeps the patient on his toes. He is taught to vary the posture of the feet slightly at frequent intervals during prolonged standing. If necessary, shortening of the tendo Achillis must be corrected.

EDITORIAL COMMENTARY—The Painful Foot

The call-up of large numbers of men and women for the Forces and for work in various heavy industrial occupations has raised the question of foot troubles in an urgent form, because there is no doubt that a large amount of disability is arising therefrom. Unfortunately there is no greater consensus of opinion now than there was before the present war started

concerning the underlying pathology of the condition which is variously described by such terms as weak foot, painful foot, foot fatigue, strained foot and so forth. The very multiplicity of names is in itself sufficient indication of the lack of agreement concerning the mechanisms involved. It is, of course, not the cases of well recognized conditions, for example hallux valgus, hammer toes, corns and the like which are the difficult ones, but that much larger group of cases in which a foot not displaying any gross deformity or disproportion nevertheless breaks down functionally when subjected to the novel demands of a new form of life. In the main there are two schools of thought on the matter, which include those who may be roughly designated the physiological (or muscular) and the anatomical (or ligamentous) adherents. Between these extremes come those who believe that both active and passive structures are involved in the development of a painful foot in varying degree. The physiological, and more modern, school believe that the primary fault is the inability of the muscular mechanism to control the posture of the foot, which results in abnormal strains being thrown upon passive structures such as ligaments, fasciae, bones and so forth—strains which it is not their normal function to sustain. The adherents of the other school, however, believe that, in the evolution of the human foot for purely locomotor purposes, a unique set of conditions has arisen; for them the failure is to be discovered primarily in the passive structures in the foot itself, the muscular effect being merely participatory and often secondary.

There are certain clinical features of the troublesome foot which both schools must recognize. In the first place, as the name implies, the pain is felt in the foot and chiefly on the plantar aspect, whereas the main muscles which could control foot posture are to be found in the calf, that is the tibial and peroneal muscles. Tenderness and swelling occur in the foot also; only rarely are they elicited in the calf. The structures which are directly responsible for the symptoms would therefore appear to be in the foot itself, and particularly in situations in which the main passive supports—such as ligaments and fasciae—are to be found. The physiological school, of course, will consider the local changes to be secondary to muscular failure. Undoubtedly one of the weak points in the older conception has been the difficulty of envisaging any process which could aptly be described as 'fatigue' in non-active tissues such as ligaments and fasciae. Recently it has been suggested, however, that the conception of fatigue in these structures may have a real pathological basis, in an autonomic reflex arising in the sensory nerve endings abundantly present in passive tissues, and that the resulting reaction of an inflammatory type would account for many of the signs and symptoms of the fatigued and painful foot. It is a great pity that the underlying cause of the condition is not more certainly understood, for efficient treatment should always be based on established pathology.

There are nevertheless certain measures with which all agree because they are founded on common sense and experience. The introduction to new and more arduous forms of occupation should not be passed through too rapidly. In the Forces the recruit has to accustom his feet to new and heavier types of footwear which by their general rigidity compel a special character of gait. If the earlier drills, route marches and exercises are not carefully graded the weaker feet will fail in this initial stage, whereas with a slower advance the great majority of feet will pass successfully through the dangerous initial period. It must be appreciated that many forms of work entail standing for long hours at a machine or bench; this immediately throws into prominence the essential difference between the foot demands of the Forces and of industry. In the former the training is essentially for activity, in the latter for inactivity. Thus the question of correct stance will be of greater importance to the industrial patient, although it should not be neglected in members of the Forces. It is much easier to state what the best stance is than to see how it could be applied in industry. A good stance is one in which the trunk is braced well back so that the centre of gravity of the body falls through the stout bones of the posterior half of the foot back to the heel, the forepart of the foot being used merely to conserve the balance. The feet should be directed straight forward and they will then naturally also fall into a position of slight inversion. Such a posture can be maintained for long periods without undue fatigue, but to advocate it in industry would be a counsel of unattainable perfection, for almost all work entails leaning forward over bench or machine. Nevertheless, a good deal of benefit might result from the education of workers in such matters, and possibly from the adoption of inclined platforms and of special footwear designed for use at the various machines or benches.

Two further points connected with painful feet deserve notice. One, which has so far received little attention, is the effect of the continued pressure ischaemia which standing still produces on localized points. This is particularly noticeable under the heads of the metatarsal bones when the stance is poor. The reactionary congestion and swelling which occur in certain other parts of the body after they have been subjected to prolonged harmful pressure are well recognized, but it is very probable that the same phenomena account for some of the pain and tenderness felt in the sole of the foot after a long shift at bench or machine. The second factor is the passive congestion which occurs in the same circumstances. In the presence of obvious varicose veins this would not escape attention, but there are many other cases in which the vascular return in the absence of muscular activity is for one reason or another imperfect, so that the feet swell after a long spell of work and in consequence become painful. Such factors add enormously to the chances of a foot breaking down when subjected to unusual strains.

The treatment of the usual painful foot is not nearly as satisfactory as many enthusiastic advocates of certain specific types of physiotherapy would have us believe; indeed in the Forces many of the persistent and severe cases can be satisfactorily dealt with only by down-grading the sufferer. By careful observations of the characteristics of feet which are prone to break down under strain, sufficient information may be collected in the future to enable medical boards to categorize feet upon recruitment, but, despite some promising attempts, we have not yet arrived at a stage at which this can be done efficiently, always excepting those gross deformities which we have already excluded from this consideration.—NORMAN C. LAKE.

- Bradley, H. (1942) *Med. Pr.*, **208**, 350.
 Discussion (1942) *Proc. R. Soc. Med.*, **36**, 47.
 Fripp, A. T. (1942) *Med. Pr.*, **208**, 347.
 Kuhns, J. G. (1942) *J. Amer. med. Ass.*, **120**, 329.
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 Nutt, J. J. (1942) *Ann. intern. Med.*, **17**, 842.

FROST-BITE AND TRENCH-FOOT

See also B.E.M.P., Vol. V, p. 440; and Cumulative Supplement, Key No. 528.

Clinical picture

Immersion-foot

Notes on a series of cases.—D R Webster, F. M. Woolhouse and J. L. Johnston in a paper read before the American Orthopaedic Association describe their observations on immersion-foot in a series of 142 cases. At the time of rescue the feet were cold, swollen and waxy white, with cyanotic areas. They were anaesthetic to pain, touch and temperature. Shortly after rescue the feet became red and hot and the swelling increased rapidly. The more severely damaged areas remained hot and oedematous and became livid in appearance. In some patients, blebs developed later on, these being filled with serous fluid or with extravasated blood. Areas of ecchymosis usually appeared. Many of the feet presented the appearance of incipient gangrene. The worst conditions occurred in natives of warm climates and in men working in the engine-room or stokehold, a fact which suggests that the defensive mechanisms are less adequate in such people than they are in those from colder climates. About the tenth day the anaesthesia was replaced by paraesthesia and neuritic pains which gradually wore off during a period of several weeks. In severe cases varying degrees of gangrene occurred. The treatment adopted was dry cooling. This was followed by rapid subsidence of oedema and absorption of the fluid in the blebs, and is thought to have reduced tissue loss to a minimum. Large doses of vitamin B failed to alleviate the neuritic pains. In some cases infective complications occurred. In all but the fifteen cases classified as severe, complete recovery took place, except for one patient who died of staphylococcal septicaemia. The average stay in hospital was 30.4 days; a short period of subsequent re-education in walking was necessary in many cases. Complete return of sensation and of motor control was sometimes delayed for many weeks. Subsequent inquiries showed that the pain is apt to recur if the feet are exposed to cold or wet or if long walks are taken. Of the fifteen severe cases seven patients recovered completely after the loss of small areas of superficial tissue, for which grafting was not required. In one case several toes and in another case one foot eventually required to be amputated.

Immersion-foot and immersion-hand

General description of the condition.—A Leading Article in the *Lancet* draws attention to the ill effects of chilling upon the feet—the so-called immersion-foot—and its importance in the Forces. In the present war the problem has arisen almost entirely in sailors. The pathology so far has been studied only in late cases in which amputation for gangrene or sepsis has been carried out, that is when secondary changes are present. Experimentally it has been shown in rabbits that the chief effect is on the blood vessels, the nerves showing only oedema of the axis cylinders without degeneration. In human cases the neuritic manifestations are much more severe. Necrosis is often superficial only, but complete gangrene may occur. The main problem is the prolonged incapacity which often follows. C. C. Ungley and W. Blackwood describe a series of eighty cases of immersion-foot and immersion-hand, which they describe as a peripheral vasoneuropathy caused by prolonged exposure to cold water. The essential cause is cold insufficient to freeze the tissues, and not wet; a similar condition was seen in the ungloved hand of an airman who had lain on a snow-covered mountain for twenty-two hours. Injudicious warming after rescue aggravated the damage; the part should be kept cool. The periods of exposure in the above series were up to fourteen days, and were occasioned by shipwreck. The immersed limbs soon became numb and felt clumsy. Swelling was observed after some hours or days. The skin was at first red, then became yellow, mottled, blue or black. The signs and symptoms observed after rescue fell into three stages. The first was the prehyperaemic stage, which lasted for a period which varied from a few hours to several days; the extremities remained cold, somewhat swollen, discoloured and numb, with glove or sock anaesthesia; peripheral arteries were sometimes pulseless at first, and remained so in cases going on to gangrene. The second or hyperaemic stage followed, sometimes lasting six to ten

weeks. The skin was hot and red, the parts were congested on hanging down and blanched rapidly when elevated. Parts going on to gangrene remained cold and a line of demarcation eventually formed. Swelling increased at first; with rest it subsided within three or four weeks. Tingling was felt, and often lasted for six weeks. Shooting pains developed at about seven to ten days, made worse by warmth and often requiring morphine. Anaesthesia persisted but areas of hyperaesthesia also might be found. There was paresis of the muscles which had end-plates within the cooled area; later wasting and impaired electrical response were noted. Anhidrosis occurred in the anaesthetic area. Blisters, ulcers or gangrene developed. The third, or post-hyperaemic stage, lasting for weeks or months, was marked by undue sensitiveness to cold, excessive sweating, hyperaesthesia and recurrent blistering. Recovery was usually more or less complete within a year, but often there were sequelae during the second year. Eighteen moderately severe cases were kept under observation for two years: two patients had been invalided, nine were doing light duty and seven full duty. The only treatment is rest. The part is kept exposed to air and dry. Sulphanilamide powder may be applied to wounds and blisters. Massage should be avoided.

EDITORIAL COMMENTARY—Tissue Damage due to Cold

It is possible to regard the many ailments which originate in part from the effects of cold as due to abnormal permeability of the capillary walls. Anything which increases capillary permeability is capable of acting as an adjuvant cause of damage and in practice it is customary to label the types of damage in accordance with the secondary and variable cause rather than with the primary common cause. The one exception is frost-bite, which is the 'straight' result of cold. The other members of the group are trench-foot, immersion-foot, shelter-foot, erythrocyanosis and chilblain.

The effects of cold on the blood vessels are fairly well understood as a result of the detailed work of T. Lewis and his associates. There is first an increased output of adrenaline which causes constriction of the vessels of the skin and extremities and thus diverts the blood to more vital structures. There is thus a transient anoxia of the affected tissues, which is, physiologically, overcome by local vasodilatation. This protecting mechanism may fail if the whole body is chilled. When thaw occurs, a gross vasodilatation takes the place of the vasoconstriction and the whole force of the arterial pressure is suddenly conveyed to the capillaries, which have already been weakened by anoxia. Excessive transudation occurs. In mild cases, damage is probably produced largely by the pressure of the oedema fluid on the venous end of the capillary bed, a state of congestion being produced. There is evidence that in more severe cases, stasis occurs. So much fluid leaves the vessels that they become silted up by stranded red cells, and are finally blocked. Gangrene of the distal tissues then occurs. Congestion may, and usually does, occur in mild degrees of cold in the neighbourhood of freezing point, and is responsible for trench-foot, immersion-foot and probably erythrocyanosis and chilblains. Stasis occurs at lower temperatures and produces true frost-bite.

The influence of nutritional deficiencies was noticed in the Crimean War, in which sufferers from scurvy suffered most severely from frost-bite. The oedema of starvation (hypoproteinaemia) and of thiamin deficiency (beri-beri) may well increase that due to cold. Scurvy, as H. Scarborough (1940) has shown, is a mixed deficiency disease, in which the ecchymoses are probably due to lack of ascorbic acid and the petechiae to lack of vitamin P. The exact relation of these two vitamins to capillary fragility and permeability is not yet clearly understood. In the past much stress has been laid on calcium deficiency, especially in the discussion of chilblains and of the localized oedema of allergic conditions. It seems that the importance of calcium has been greatly exaggerated. There is no correlation between the occurrence of chilblains and of known disorders of calcium metabolism and the therapeutic application of calcium has proved useless.

Circulatory stagnation increases transudation by increasing venous pressure. It may be produced by tight clothing, especially socks and garters, or by pressure on the popliteal space by the hard edge of a chair. Wind increases evaporation and thus cools the skin. It also blows away the warm layer of air about the body. Anoxia, usually encountered at great altitudes on mountains or in airplanes, increases capillary permeability. It reduces still further the oxygen supply to the damaged tissues, partly because the blood is insufficiently oxygenated and partly because the minute volume of the heart is reduced. Lesser degrees of anoxia, occurring in anaemia, heart failure, respiratory disease and shock may contribute to the occurrence of frost-bite. Damp is the predominant subsidiary cause of trench-foot and immersion-foot, in which it acts in virtue of its thermal conductivity. It may be a factor in the development of true frost-bite because of its power to reduce the capacity of the skin to supercool. Warmth and exercise after damage has occurred are harmful, because they produce hyperaemia and thus increase the strain on the capillary walls.—RAYMOND GREENE.

Leading Article (1942) *Lancet*, 2, 457.

Ungley, C. C., and Blackwood, W. (1942) *Lancet*, 2, 447.

Webster, D. R., Woolhouse, F. M., and Johnston, J. L. (1942) *J. Bone Jt Surg.*, 24, 785.

GALL-BLADDER AND BILE-DUCTS

See also B.E.M.P., Vol. V, p. 477.

Diseases of bile-ducts

Obstruction

Pathological physiology of the common bile-duct.—Under the above title the seventeenth Lewis Linn McArthur lecture was given at the Frank Billings Foundation in 1941 by W. Walters, of the Mayo Clinic, who first quotes from the writings of his colleague, A. M. Snell, on the mechanism of emptying of the gall-bladder and common bile-duct. All the available evidence shows that the gall-bladder fills in an interdigestive phase and that after a meal its contents are discharged into the duodenum. The extrahepatic and the common bile-duct are largely passive tubes, but the latter terminates in that complex sphincteric mechanism, the ampulla of Vater, which regulates the evacuation of the gall-bladder. After cholecystectomy the sphincter becomes incompetent and the bile dribbles into the duodenum exactly as it does in species of animals without a gall-bladder; later the sphincter regains tone and may be responsible for some of the dilatation of the extrahepatic bile-ducts. A. C. Ivy and E. Oldberg extracted from the duodenal mucosa a substance cholecystokinin, which, when injected intravenously, brought about normal contraction of the gall-bladder and evacuation of its contents. In human beings the above hormone is secreted after the introduction of acids and fats into the duodenum; egg yolk and cream are the most effective stimulants, proteins come next, whereas carbohydrates have little or no effect. Walters arranges the causes of obstruction of the common bile-duct in the following order of frequency: (1) gall-stones, (2) inflammation in the wall of the duct and in the pancreas, (3) new growth of the duct, the ampulla and pancreas, and (4) functional obstruction, the result of spasm of the sphincter of Oddi and of the duodenum. In answer to the question: Should the surgeon open and explore the common bile-duct in all cases in which operations are performed on the gall-bladder? Walters's reply is 'Certainly not'. Inflammatory obstruction of the common duct occurs oftener than is realized. In about 75 per cent of cases of inflammatory obstruction of the common bile-duct, with or without calculi, Gram negative bacilli are found in combination with streptococci and staphylococci. Reference is made to V. C. Hunt and J. W. Budd's collection of seventy-six cases of radical operation for primary carcinoma of the ampulla of Vater, with an operative mortality of twenty-nine, or 38 per cent; but the prognosis after the radical operation is better than that for pancreatic carcinoma. Attention is drawn to E. A. Boyden's work on Oddi's sphincter and to the value of thorough drainage in biliary obstruction, and of cholangiography in the demonstration of retained calculi.

Carcinoma of bile-ducts

Diseases around the biliary papilla and ampulla of Vater.—In a Hunterian lecture given on 18th June, 1942 at the Royal College of Surgeons of England, G. Gordon-Taylor dealt mainly with two aspects of a subject complicated by the possible origin of disease in at least four sites closely adjacent to each other, namely primary carcinoma of the mucosa of the ampulla of Vater or the head of the pancreas, of the lower end of the common bile-duct, of the main pancreatic duct, and of the duodenal surface of the biliary papilla. From the above origins primary carcinoma may spread to one or more of the other possible origins so that the original starting-place is obscured. The two parts of this Hunterian lecture deal with (1) the radical surgery of cancer of the lower end of the common bile-duct and in that region, and (2) the sphincteric arrangement of the terminal part of the common bile-duct. Gordon-Taylor quotes examples of these forms of primary carcinoma and mentions eight cases of his own. The growths are described as being of low malignancy. In connexion with the sphincter mechanism of the lower end of the common bile-duct, Gordon-Taylor points out that Francis Glisson, Regius Professor of Physic at Cambridge from 1634 to 1677, preceded Oddi and his work on this subject by 250 years; but neither of their two descriptions is accepted as accurate. The different opinions about the existence of a special intrinsic sphincter and the work done by J. Kirk are reviewed. Evidence is quoted in favour of the presence of a special intrinsic sphincter at the terminal portion of the common bile-duct or of the conjoined bilio-pancreatic duct. The muscular sheath of the common bile-duct is derived from the circular muscular coat of the duodenum, but the muscular fibres found around the basal portion of the intramural bile-duct are not circular, being only longitudinal and oblique in the distal portion of the papilla. The action of these fibres is partly to retract the papilla and partly to erect or to aggregate the villous processes centripetally, thereby preventing reflux from the duodenum and controlling the exit of bile.

Boyden, E. A. (1937) *Surgery*, **1**, 25.

Gordon-Taylor, G. (1942) *Brit. med. J.*, **2**, 119.

— (1942) *ibid.*, **2**, 149.

Hunt, V. C., and Budd, J. W. (1935) *Surg. Gynec. Obstet.*, **61**, 651.

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GAS GANGRENE

Treatment

X-ray therapy

Experimental observations.—E. Singer has tried to estimate the value of X-ray therapy in gas gangrene by using it in mice inoculated with cultures of *Clostridium welchii* or of *Vibrio*

septicaemia. Two sets of tests were arranged; in one X-ray treatment was used alone and in the other it was combined with local injection of sulphanilamide. The infecting dose of organisms was the amount which in control experiments had been found to kill every mouse within twenty-four hours when given alone, but which killed only some of the mice when sulphanilamide was injected simultaneously. The X-ray treatment consisted in one or two exposures of nine or eighteen minutes. The animal was first fixed in position, the injection was given and X-ray treatment was begun. The results were entirely negative since, neither alone nor in combination with sulphanilamide, did irradiation affect the survival rate of the mice. The author suggests that at least some of the enthusiastic clinical reports may be accounted for by the fact that gas-forming organisms can often be demonstrated as saprophytes in wounds which do not show any sign of gas gangrene; such wounds would heal without any treatment. On the other hand, wounds which harbour a mixed flora in which gas gangrene organisms have a chance to develop might react favourably to X-ray therapy, and gas gangrene might thus be prevented.

Singer, E. (1942) *Med. J. Aust.*, **2**, 1

GASTRITIS

See also B.E.M.P., Vol. V, p. 533.

Morbid anatomy and pathology

Macroscopic appearances

Experimental tuberculous gastritis in dogs—The rarity of tuberculosis of the stomach is established, but as D. C. Browne, G. McHardy and C. Wilen point out, dyspepsia is a prominent symptom in a large proportion of cases of pulmonary tuberculosis. The authors endeavoured to produce tuberculous gastritis in the dog. A static gastric pouch was first constructed in either the cardia, the fundus or the pyloric part, and a virulent culture of tubercle bacilli was afterwards introduced either directly into the submucosa of the pouch or by injection into the gastro-epiploic artery. The mucosa was deliberately injured at the time of the injection. It was found that neither in the cardiac (achylic) pouch nor in the fundal pouch, containing free hydrochloric acid, did any significant lesions develop. In the pyloric pouch tuberculous lesions, ulcerative or proliferative, were produced by either method of inoculation. The authors have also examined a series of bodies of patients who died of pulmonary tuberculosis, and they found evidence of tuberculous gastritis in 5.8 per cent and of simple gastritis in 46.8 per cent. In a series of fifty consumptives examined gastroscopically no specific lesions were discovered, but the mucosa was normal in only 34.7 per cent. Atrophic and superficial gastritis and ulceration were found in the remaining patients.

Macroscopic and microscopic appearances

Fifty-one resected stomachs under review.—L. B. Benedict and T. B. Mallory have made a comparative gastroscopic and histological study of pathological specimens obtained from surgically resected stomachs in fifty-one cases. The authors believe that biopsy specimens are unsatisfactory because they are too small and because they are more likely to be seriously injured during removal. The series included twenty-three cases of ulcer, twenty-two of carcinoma, two of pure gastritis, two of lymphoma and one of benign polypus. One stomach was normal. In only six cases did the pathological and gastroscopic findings conflict with regard to the presence and type of gastritis.

Benedict, L. B., and Mallory, T. B. (1943) *Surg. Gynec. Obstet.*, **76**, 129.

Browne, D. C., McHardy, G., and Wilen, C. (1942) *Amer. J. digest. Dis.*, **9**, 407.

GLAUCOMA

See also B.E.M.P., Vol. V, p. 575.

Primary glaucoma

Treatment

The results of surgical treatment—S. A. Fox analyses some of the results of the surgical treatment of glaucoma carried out during the five-year period ending in 1939 at the Bellevue Hospital, New York. Excluding paracentesis and posterior sclerotomy, 234 major operations were performed for all types of increased intra-ocular pressure. The results in fifty-four cases of primary glaucoma were selected for study because complete data for these cases were available. There were thirty-one cases of chronic congestive glaucoma, twelve of chronic simple glaucoma and eleven of acute congestive glaucoma. All patients have been observed subsequently for at least six months, and thirty-three were kept under close observation for from two to six years. Of the thirty-one cases of chronic congestive glaucoma, in twenty-two (70.9 per cent) the tension was reduced to normal, that is to 25 millimetres Hg or less, after operation. Vision, however, was the same or better in only seventeen cases (54.8 per cent) and the visual fields were maintained in only thirteen (41.9 per cent). Moreover the condition of the patients observed for from three to six years was worse in all respects than that of those seen for two years or less. Deterioration appears to be a constant feature of glaucoma in patients surgically treated. In the twelve cases of simple chronic glaucoma the results were slightly better but showed the same deterioration as time progressed. The percentages of patients with normal tension, with vision the same or better and with fields the same or better

were 75.0, 58.3 and 50.0 respectively. Of the eleven cases of acute glaucoma normal tension was maintained in eight (72.7 per cent). In the whole series normal tension was maintained in thirty-nine cases (72.2 per cent) with or without miotics. As far as the evidence of this small series goes, the results were better in acute glaucoma treated by iridectomy than in chronic glaucoma treated by trephining or sclerectomy. In a few cases of acute glaucoma iridotomy or cyclodialysis was performed; the results of the former method were better and those of the latter were worse than those of iridectomy, but final conclusions cannot be drawn from such small numbers of cases. From the literature of the past fifteen years the conclusions can be drawn that the iris-inclusion technique is gaining in popularity but that otherwise little progress has been made and that unanimity has not been reached regarding the best method of treatment.

I-ox, S. A. (1943) *Amer. J. Ophthalm.*, **26**, 31.

GOITRE AND OTHER DISEASES OF THE THYROID GLAND

See also B.E.M.P., Vol. V, p. 599, and Cumulative Supplement, Key Nos. 569–574.

Pathology of the thyroid gland

Involution

Senile changes.—W. Andrew and Nancy V. Andrew point out that work on the senile changes in the thyroid gland is not wholly lacking but that both observations and interpretations are often at variance. This may be due, at least in part, to the fact that usually the human gland has been studied and with this it is not then so often possible to eliminate factors of malnutrition, race and environment, and pathological conditions, as with experimental animals. The authors therefore confined their observations to one animal, the mouse, mainly the pedigreed black mouse. Twenty mice were used and were divided into three groups, the young, the middle-aged and the senile. After a short residence in the laboratory the mice were killed by rapid etherization, and the thyroid gland, together with the attached larynx, was cut into sections of from 8 to 10 μ . The glands in the three age groups show qualitative and quantitative differences which are greater between middle-aged and senile animals. In the young animals the follicles are relatively small, the epithelial cells are cuboidal and the colloid is almost homogeneous. There is a fairly large amount of interfollicular material, consisting chiefly of immature adipose tissue. In the middle-aged group of mice the follicles are larger, with low-cuboidal or squamous epithelium, homogeneous colloid, and very little interfollicular connective tissue. In senility there is an enormous increase in the fibrous tissue between the follicles, some of which are atrophied, others overdistended. The colloid varies greatly; many follicles are devoid of staining colloid, entirely or partly, others show granular change, stratification and fissures. Though senile changes of the same kind occur in both sexes, they are more advanced in female than in male mice in senility.

Toxic goitre

Pathology

Vitamin B complex and glycogen metabolism.—V. A. Drill, R. Overman and C. B. Shaffer have studied the relation between thyroid gland function and the B vitamins by feeding groups of rats, rendered hyperthyroidic by administration of thyroid extract, on diets containing varying amounts of yeast products. In a control group, rats which had not received any thyroid extract and were given 200 milligrams (3 grains) of yeast a day gained weight; when they were killed at the end of the experiment the liver glycogen values were normal (average 2.51 per cent). Of the rats fed on thyroid extract, one group was given 200 milligrams of yeast daily, a second group was given in addition 1 gramme (15 grains) of a yeast concentrate. The animals in the first group all lost weight and the liver glycogen was found to average only 0.34 per cent when they were killed. The rats in the second group gained weight and normal liver glycogen amounts (average 2.20 per cent) were found after death. The effect of vitamin B appears to be to stimulate appetite and thus to increase food intake; this serves to compensate for the increased utilization of glucose by the tissues and the consequent depletion of glycogen reserves which occurs in hyperthyroidism.

Andrew, W., and Andrew, Nancy V. (1942) *Amer. J. Path.*, **18**, 849.

Drill, V. A., Overman, R., and Shaffer, C. B. (1942) *Endocrinology*, **31**, 245.

GONORRHOEA

See also B.E.M.P., Vol. VI, p. 1; and Cumulative Supplement, Key Nos. 575–578.

Gonorrhoea in males

Treatment

Chemotherapy and induced pyrexia.—R. C. L. Batchelor, G. M. Thomson and J. L. Huggan have treated more than twenty patients with gonorrhoea, who had failed to respond to treatment by sulphapyridine, by the combined use of sulphapyridine or sulphathiazole and induced pyrexia. The routine is as follows: First day: from 6 to 8 grammes (90 to 120 grains) of sulphapyridine is given intravenously in divided doses of 2 grammes (30 grains). Second day: 2 grammes of sulphapyridine orally; a minimum of eight hours in the inductotherm cabinet, with fever of over 106° F., during which a further 6 or 8 grammes of sulphapyridine is given orally or, if necessary, intravenously. Next five days: sulphapyridine, from 4 to 6 grammes

(60 to 90 grains) daily unless severe vomiting sets in. Renal complications have not occurred, a fact which the authors attribute to the large fluid intake resulting from the thirst induced by the fever. The successes resulting from the treatment approach 100 per cent.

Prevention and treatment.—The importance of prevention of venereal disease is stressed by J. C. Booth. At his clinic prophylaxis for males is available for twenty-three hours out of the twenty-four. The method used is irrigation of the anterior urethra with potassium permanganate solution, 1 in 6,000, and the application of calomel ointment to the external genitalia and adjacent parts. In cases of established infection the method of treatment in use is as follows. Sulphapyridine is given in doses of 1 gramme (15 grains) three times a day for five days, with subsequent doses of 0.5 gramme (8 grains) three times a day for five days. The discharge usually ceases within forty-eight hours; if it persists for five days (which occurs in about 20 per cent of cases) irrigation with potassium permanganate is begun, and is continued concurrently with the course of sulphapyridine treatment, and afterwards for as long as may be necessary. If the discharge persists for a two-week period during which sulphapyridine is not given, the course is repeated. In some cases a vaccine has been used between courses of sulphapyridine. When response is satisfactory tests for cure are begun as soon as chemotherapy ceases. The patient is discharged only if repeated bacteriological tests are negative, and if serological evidence of gonorrhoea or syphilis is lacking. If the serological test for gonorrhoea is positive but search and provocative treatment fail to show a focus, the patient is asked to report for further testing in three months' time. The serological test may continue positive for as long as two years after signs of active infection have subsided. Complications mostly require in-patient treatment.

Batchelor, R. C. L., Thomson, G. M., and Huggan, J. L. (1942) *Ednh. med. J.*, **49**, 584.

Booth, J. C. (1942) *Med. J. Aust.*, **2**, 292.

GOUT

See also B.E.M.P., Vol. VI, p. 37, and Cumulative Supplement, Key No. 579.

Treatment

Use of vitamin B₁

P. Roenne, in a personal communication with regard to the treatment of gout with vitamin B₁, says that for over a year he has employed the following method. When an attack begins he injects intravenously 10 milligrams of vitamin B₁ or alternatively 20 milligrams intramuscularly at the outer gluteal region, if the patient is not suitable for intravenous treatment. Sometimes only one injection is required. At the same time the patient receives daily by the mouth 12 milligrams of vitamin B₁ tablets, not only during the acute stage but also for some time afterwards. Attention is paid to diet and patients in the acute stage are given also a mixture containing colchicum and pyramidon. Roenne sums up the value of vitamin B₁ in gout by saying (1) that attacks of gout are aborted when vitamin B₁ is given early on, some attacks lasting less than a day; (2) that the frequency is less as compared with previous years, and this despite numerous indiscretions on the part of the patients with regard to food and drink, also neglect to continue the taking of vitamin B₁ tablets as a prophylactic measure; (3) that one patient who used to have attacks every three or four months has been free for nine months. Roenne says that since gout is due to disturbances of the metabolism, in susceptible persons vitamin B₁ helps to put carbohydrate metabolism right and it also breaks down nucleotids.

Diet

Low-fat high-carbohydrate diet.—A plan of treatment for gout is described by E. C. Bartels. Thirty-one patients carried out the treatment. The number of acute attacks was reduced to seven minor as compared with eighty-four major attacks during an equal period of time before treatment was started. The average uric acid level in the blood fell considerably. The diet prescribed was low in purine bodies and fats, and high in carbohydrates. The reason for restricting fats was that a high fat diet has been shown to promote retention of uric acid. Cincofen was given as an adjunct to the diet in doses of 7½ grains (0.5 gramme) three times a day for three days a week, but was then reduced and was finally omitted as the serum uric acid approached normal levels. To obviate the risk of poisoning, tests of liver function were made at intervals and if the results fell below normal the drug was stopped; patients were instructed in the recognition of the early symptoms of poisoning.

Bartels, E. C. (1943) *Ann. intern. Med.*, **18**, 21.

Roenne, P. (1943) Personal communication.

GUINEA-WORM DISEASE

See also B.E.M.P., Vol. VI, p. 61; and Cumulative Supplement, Key No. 581.

Definition and aetiology

Geographical distribution

In Osmanabad.—S. R. Rao reports the results of a survey of the Osmanabad district carried out in 1937 to ascertain the prevalence of guinea-worm disease in the area. Ninety-one representative villages were visited and a house to house inquiry was made. The wells of the villages

were examined for cyclops, and were disinfected with lime if parasites were found. Two towns only in the district possess up to date plants for water supply. The entire area was found to be heavily infected. For the whole district the number of cases averaged 28.9 per thousand; in several places the number suffering from the disease was found to reach 10 per cent of the population, and the number who had suffered from it in the past had reached 80 per cent. Men were affected more often than women, and young adults more than those in other age groups. The average duration of the illness is about a month in uncomplicated cases but it may drag on for months if sepsis supervenes. Repeated attacks can occur; the highest number noted in a single individual was fifty. The loss to the agricultural workers is serious, because the working members of a family are disabled just when their labour is badly needed in the fields. Moreover permanent disability, for example an ankylosed knee, may result. The prevalence of the infection results from infestation of the majority of the wells; many are step wells of antiquated design or are unprotected draw wells. Disinfection with lime was found to be of little use, subsequent examination showing that cyclops invariably reappeared in the water after an interval which, in some instances, was as short as one week; quicklime is more effective than are other forms of lime. Proper water supplies are essential if the disease is to be controlled, and in the meantime regular disinfection of wells with lime is recommended.

Rao, S. R. (1942) *J. Indian med. Ass.*, **11**, 329.

HAEMATOPORPHYRINURIA

See also B.E.M.P., Vol. VI, p. 85.

Clinical

Association of alcoholic cirrhosis of liver and coproporphyrinuria

Coproporphyrin in the urine.—S. Nesbitt continues his work on the excretion of porphyrin which as he had previously shown probably arises in the body during the process of the synthesis of haemoglobin. He now reports four cases of severe alcoholic cirrhosis of the liver in which he demonstrated that there is a close correlation between the values for urinary coproporphyrin excreted daily and for the corresponding urinary volume, and that these values bear a definite relation to the onset and the course of periods of acute hepatic insufficiency. The episodes of repeated acute hepatic insufficiency were shown by periods of neurological symptoms ranging from mild disorientation and psychotic behaviour to deep coma. In each of the patients the amount of the urinary coproporphyrin excreted was estimated daily; this was surprisingly parallel to the corresponding volume of urine, and it was seen that before and during each episode of acute hepatic insufficiency there was a sharp decline in the amount of the urinary coproporphyrin as well as in the volume of the urine. Further, these values increased abruptly as the patient emerged from the acute episode.

Nesbitt, S. (1943) *Arch. intern. Med.*, **71**, 62.

HAEMATURIA

See also B.E.M.P., Vol. VI, p. 97; and Cumulative Supplement, Key Nos. 585 and 586.

Aetiology

Significance of other urinary abnormalities

Haematuria after sulphadiazine.—D. O. Wright and R. E. Kinsey have observed seven cases of renal complications among a total of thirty-eight patients treated by sulphadiazine. The number of days during which the drug had been given varied from one to eleven. The fluid intake appeared to be adequate but the output was low in every case owing, it is supposed, to hot weather. The urine in all cases had been normal up to the onset of haematuria, and was acid in reaction. Renal tenderness was a constant finding before the onset, and indeed it may be a valuable danger signal. Crystalluria was present in four cases before and during the haematuria. The authors believe that sulphadiazine causes two types of renal damage, one due to mechanical blockage, the other due to poisoning of the tubular epithelium, and that this accounts for the absence of crystals in three cases, in one of which the urinary output was low and the blood non-protein nitrogen was high for several days after haematuria, had ceased. All the patients responded to conservative treatment, in which fluids, alkalies, sedatives and local heat were given.

Wright, D. O., and Kinsey, R. E. (1942) *J. Amer. med. Ass.*, **120**, 1351.

HAEMOGLOBINURIA

See also B.E.M.P., Vol. VI, p. 115; and Cumulative Supplement, Key Nos. 588–593.

Clinical picture

Paroxysmal haemoglobinurias

Acute paralytic myohaemoglobinuria in human being.—E. G. L. Bywaters and J. H. Dible give a comprehensive review with abstracts of the seven previously reported cases, and describe what they regard as an eighth case of spontaneous myohaemoglobinuria, resembling that seen in the horse and in Hafl's disease. In only two of the seven cases was myohaemoglobin identified, but the combination of severe muscular damage, evident clinically or found on pathological examination, with haemoglobinuria without signs of haemolysis, was considered

to justify the diagnosis; the close resemblance to equine paralytic myohaemoglobinuria is another argument with the same bearing, as is the similarity to Haff's disease in which H. Assmann, H. Bielenstein, H. Habs and B. zu Jeddelloh, reporting on a case in a man, identified the urinary pigment as myohaemoglobin. The damage to muscles may be direct as in the crush syndrome, or it may be due to some product found in fish from water contaminated by industrial effluents. The authors' case of idiopathic myohaemoglobinuria was clinically one of acute nephritis and, although with some resemblance to acute porphyria, the view that it is of that nature is not accepted. The voluntary muscles showed much patchy loss of pigment and some diminution in the intensity of the transverse striations. The renal changes in the authors' case showed fibrosis around the second convoluted tubules and resembled the histological lesions seen in the crush syndrome.

Assmann, H., Bielenstein, H., Habs, H., and zu Jeddelloh, B. (1933) *Dtsch med. Wschr.*, **59**, 122.

Bywaters, F. G. L., and Dible, J. H. (1943) *J. Path. Bact.*, **55**, 7.

HAEMOPHILIA

See also B.E.M.P., Vol. VI, p. 123, and Cumulative Supplement, Key No. 594

Treatment

Treatment of attack

Clarification of principles—C. L. Endicott, J. H. Mitchell and G. Qvist record the case of a haemophilic, aged thirty-five, with a history of attacks of bleeding since the age of nineteen, who died from asphyxia due to bleeding after dental extraction, the massive haemorrhage occurring into the submucosa of the floor of the mouth. A note is added on the spread of infection in Ludwig's angina in which involvement of the mylohyoid muscles plays an important part. R. G. Macfarlane and L. J. Witts insist on the unfamiliarity, as shown by Endicott, Mitchell and Qvist's paper, of the principles of the treatment of haemophilia, and hope that the facts of the case will discourage such measures in the future. G. G. Turner recommends the local treatment for bleeding from a tooth socket, of a turpentine-soaked plug dressing which invariably arrests the haemorrhage.

Endicott, C. L., Mitchell, J. H., and Qvist, G. (1942) *Brit. med. J.*, **2**, 34.

Macfarlane, R. G., and Witts, L. J. (1942) *Brit. med. J.*, **2**, 140.

Turner, G. G. (1942) *Brit. med. J.*, **2**, 258.

HAEMORRHAGIC DISEASES

See also B.E.M.P., Vol. VI, p. 138.

Hereditary haemorrhagic disorders

Neonatal haemorrhage

Effects of antenatal administration of vitamin K—A study by J. Parks and L. K. Sweet of the effects of antenatal administration of vitamin K leads them to the conclusion that the incidence of neonatal haemorrhage is unaffected thereby. A group of 1,151 mothers, on admission to the obstetric ward, each received a single oral dose of 5 milligrams ($\frac{1}{2}$ grain), while a control group of 1,594 mothers did not receive any vitamin K. The prothrombin level of the mother's blood was estimated on admission and that of the umbilical cord blood was estimated at the time of delivery. In the patients who received vitamin K the umbilical cord blood level was about 20 per cent higher than it was in the untreated group. Despite the above fact, gross abnormal bleeding (only serious cases being counted) was noted in 1.7 per cent of the infants of women in the treated group; in the control group the percentage was 1.4. At least one-third of the mothers, however, entered hospital too late for the drug to be likely to exert any effect.

Parks, J., and Sweet, L. K. (1942) *Amer. J. Obstet. Gynec.*, **44**, 432.

HAND, DISEASES AND DEFORMITIES

See also B.E.M.P., Vol. VI, p. 171; and Cumulative Supplement, Key Nos. 613-617.

Injuries

Treatment

General management of the case.—The importance of wounds of the soft tissues of the hand depends mainly upon the stiffness of the small joints to which they may lead. B. K. Rank for this reason urges that the greatest care should be given even to small wounds in order to control infection and hasten healing and thus to minimize the formation of scar tissue. Skin grafting is indicated in the hand for much smaller areas than in other regions. Temporary pinch grafts or split skin grafts may be of value in the early stages even although they may later have to be replaced by a better type of graft. Initial debridement should be as conservative in the hand as in the face. Early function is essential and immobilization of any part of the hand should be for as brief a time as possible. Baths and assisted movements are of great value for hand wounds. The typical example of injury in which soft tissues are chiefly involved is the 'hand grenade' wound. Such wounds usually heal quickly under adequate treatment but often leave much residual disability from scarring. Free excision of the scars and replacement by Wolfe grafts offer a good prospect of a useful hand. The excision must

be so planned that any possible scarring about the edges of the graft will not produce the original disability and this often means removal of some normal skin. The dissection should be done in a bloodless field and absolute haemostasis must be secured before the graft is applied. Ligatures should be used as sparingly as possible and chief reliance placed on heat and pressure. The graft must be free from fat and its edges carefully sutured to the edges of the defect. A pressure dressing is applied and left undisturbed for from ten to fourteen days unless signs of circulatory embarrassment appear. At the first dressing the stitches are removed, the edges of the graft are painted with mercurochrome and a fresh pressure dressing is applied. Movements may be started but pressure dressings must be maintained until three weeks have elapsed. Ulcers which may appear on the graft are treated with mercurochrome. Wounds of the 'through and through' type usually result in more damage to bones and tendons and greater stiffness of joints. The principles of treatment are the same, but it is usually better to use a direct abdominal flap of skin and fat to cover sutured tendons.

Rank, B. K. (1943) *Aust. N.Z. J. Surg.*, **12**, 191

HEADACHE

See also B.E.M.P., Vol VI, p. 199

Types of headache

Migraine

Clinical types of migrainous headache.—Headaches of a migrainous type are divided by G. F. Rowbotham into two groups as follows. (1) Associated with an organic lesion of the brain. (2) Associated neither with local cerebral change nor with gross metabolic disturbance. The latter group only should be counted as true migraine. The sites at which the painful impulses originate are thought to be the arteries of the scalp and dura mater, for the following reasons: when an operation is performed under local anaesthesia, crushing of the trunk or a large branch of the middle meningeal artery causes extreme discomfort, spasm of the common carotid artery, observed in similar circumstances, was associated with severe pains on the same side in the head and face, forcible distension by injection of saline into a large artery of the scalp causes pain, migraine is accompanied by signs of vasoconstriction; ergotamine tartrate relieves migraine, headache can be induced by histamine. The pathway by which the painful impulses reach the cerebral centres appears to be the posterior root of the trigeminal nerve, which the author has divided in three cases of migraine, conferring complete relief. The route by which painful impulses enter the Gasserian ganglion is problematical.

Rowbotham, G. F. (1942) *Brit. med. J.*, **2**, 685.

HEART DISEASES: EXAMINATION

Systolic murmurs

Diagnostic significance

Causes.—The diagnostic value of a systolic murmur is discussed by W. Evans under the following headings. (1) The irrelevant murmur. Such murmurs do not signify mitral disease and are usually loudest at some other auscultatory site. They include the conducted murmurs of congenital pulmonary stenosis, patent ductus arteriosus and defects of the interventricular septum, the haemic murmur of anaemia, the murmur associated with cardiac displacement; the murmur accompanying tachycardia. (2) The innocent murmur. This is short and except when occurring late in systole is not loud. It is usually decidedly louder when the patient is in the upright position and often disappears during inspiration and diminishes with increase of the heart rate. (3) The murmur of mitral incompetence. Mitral incompetence is a condition so difficult to diagnose with certainty that the term should be abandoned, and any mitral systolic murmur not falling under either of the two foregoing heads should be classed as a concomitant of one of the following, mitral stenosis, aortic stenosis, aortic incompetence, hypertension, cardiac aneurysm or the cardiac enlargement associated with heart block. This type of systolic murmur is moderately loud, best heard when the patient is in the reclining position and increasing with increased heart rate. Naturally other signs will be taken into account in assessing the significance of any cardiac murmur.

Electrocardiographic investigation

Effect of posture

In normal subjects.—H. S. Mayerson and W. D. Davis, Jun. discuss electrocardiographical changes which accompany change of posture. Series of readings were taken from ten normal subjects before, during and after passive tilting. By this method the influence of muscular action in aiding venous return is eliminated and the load on the circulatory system is increased. The subjects fell into three groups. (1) those showing an accelerated pulse and a rise in diastolic pressure with unchanged systolic pressure, able to maintain the upright position for twenty minutes without discomfort; (2) those with more pronounced tachycardia and a rise in diastolic, often associated with a fall in systolic, pressure, who usually fainted; (3) those of an intermediate type, who showed tachycardia, pallor and sweating but did not actually faint. The chief findings were increased amplitude of the P wave in leads 2 and 3, decreased amplitude of the T wave, shift of the average QRS axis to the right and of the average T axis to the left and decrease in the QRST area. The immediate response to the upright posture

probably signifies a change in the heart's position. In some subjects the changes continued to develop during the entire upright period. This is thought to indicate increased sympathetic activity secondary to reduced venous return with relative cerebral anoxia.

Effects of various factors

Interpretation of records.—A. S. Hartwell, J. B. Burrett, A. Graybiel and P. D. White have studied electrocardiographical changes produced by various agents in five healthy men, aged twenty-one to thirty-eight years, all of whom had normal electrocardiograms. Each experiment was preceded by a period of rest until the pulse and the blood pressure were steady. The following methods were used. (1) *Exercise*. Electrocardiograms were taken before, during and immediately after a period of exercise on a bicycle-machine. It was found that exercise lowered the T wave in lead 2 in all subjects, with return to normality within a minute; during the recovery period the T wave was sometimes bigger than the normal. (2) *Adrenaline*. 1 in 1,000 adrenaline hydrochloride solution was injected subcutaneously, four of the subjects receiving 1 cubic centimetre, the fifth being given 0.5 cubic centimetre. Electrocardiograms taken five, ten, fifteen, twenty and thirty minutes afterwards showed a lowering of the T wave in all subjects, which persisted for from fifteen to thirty minutes. (3) *Ergotamine tartrate*. Two subjects received 1 cubic centimetre, the others 0.5 cubic centimetre, of ergotamine tartrate 1 in 1,000 solution, and tracings were taken five, fifteen, thirty and, in three of the subjects, sixty minutes later. The T wave was raised in each tracing, the effect lasting for an hour. (4) *Atropine sulphate*. Subcutaneously $\frac{1}{10}$ grain (0.0012 gramme) was given and electrocardiograms were taken twenty, forty, sixty and ninety minutes later. The T wave was lowered in all subjects for a period of up to ninety minutes. (5) *Acetyl- β -methylcholine chloride*. Two subjects were given 25 milligrams ($\frac{1}{2}$ grain), the others 15 milligrams ($\frac{1}{4}$ grain), subcutaneously. The T wave was lowered in all subjects, and in all tachycardia developed without preliminary bradycardia. (6) *Right carotid sinus pressure*. The effect of this was studied in four subjects, all showed slowing of the pulse with increased T waves. The authors emphasize the importance of taking into account various factors, including autonomic influences, when interpreting electrocardiograms.

Evans, W. (1943) *Brit. med. J.*, **1**, 8.

Hartwell, A. S., Burrett, J. B., Graybiel, A., and White, P. D. (1942) *J. clin. Invest.*, **21**, 409.

Mayerson, H. S., and Davis, W. D., Jun. (1942) *Amer. Heart J.*, **24**, 593.

HEART DISEASES: CONGENITAL DISEASES

See also B.E.M.P., Vol. VI, p. 206; and Cumulative Supplement, Key Nos. 619–635.

Coarctation of the aorta

Adult type

Fatal rupture of the aorta.—R. C. Black reports a case of coarctation of the aorta terminated by rupture of the proximal part of the vessel at the age of twenty-one. The subject, a garage hand, was found dead in a lavatory. Necropsy was performed, and the findings were as follows. The pericardium was greatly distended with blood and soft clot. The left common carotid artery was of much smaller calibre than was the right and from its origin onward the lumen of the aorta was reduced to one of less than five millimetres in diameter. A longitudinal rupture three centimetres long was present in the first part of the aorta, microscopically the intima here appeared normal. A patent ductus arteriosus was present. The left ventricle was slightly hypertrophied. It is presumed that rupture took place as the result of straining at stool and consequent further increase in the high pressure which must have been present in the first part of the aorta.

Black, R. C. (1942) *Med. J. Aust.*, **2**, 178.

HEART DISEASES: RHEUMATIC HEART DISEASE IN CHILDREN

See also B.E.M.P., Vol. VI, p. 234; and Cumulative Supplement, Key No. 636.

Course and prognosis

Fatal cases

Mortality statistics.—Observations in connexion with the prognosis of rheumatic carditis have been made by T. F. Cotton on the histories of 200 boys observed over a ten-year period. The average age at the onset of the illness was eleven years. The children were under treatment in a special home and were divided into two equal groups, for one of which the average stay was four and a half months, for the other six months. It could not be said that the longer stay improved the outlook. At the end of ten years, of the first group 54 per cent were living, 40 per cent were dead and 6 per cent could not be traced; of the second group the figures were 49 per cent living, 34 per cent dead and 17 per cent untraced. Twenty-one of the children died within five years and eighteen within the second five years. In the combined groups mitral stenosis carried a higher mortality than did mitral regurgitation, and aortic regurgitation plus mitral stenosis had the heaviest mortality rate (50 per cent). The death rate was less in children with little or no enlargement of the heart than in those whose heart was moderately or much enlarged when they came under observation. The correlation of signs of activity with those of structural damage to the heart is an essential basis for prognosis and treatment.

The temperature and pulse chart and the erythrocyte sedimentation rate are the most reliable guides in assessing the activity of the rheumatic process. In children loss of weight or failure to gain weight is suggestive. Heart signs are less helpful. Partial heart block, as shown electrocardiographically by a lengthened P-R interval, is common and may outlast all other manifestations of active infection for months. Auricular fibrillation is a sinister sign, denoting the likelihood of death within three years.

Cotton, T. F. (1942) *Brit. med. J.*, **2**, 473.

HEART DISEASES: ENDOCARDITIS MALIGNANT

See also B.E.M.P., Vol. VI, p. 297; and Cumulative Supplement, Key Nos. 644-646.

Subacute bacterial endocarditis

Aetiology

Atypical micrococci.—J. B. Penfold reports two cases, of acute and of subacute endocarditis respectively, due to atypical micrococci which could not be identified with any known species. Probably they were nearest in type to *Staphylococcus albus*, but they differed from it in some respects. The classification of staphylococci and micrococci is still tentative and unsatisfactory; there is much confusion in the terms used and many kinds of organism causing bacterial endocarditis have been labelled *S. albus*; the term *S. aureus* should be dropped and in its place *S. pyogenes* could cover organisms producing either yellow or white colonies, but whose characteristics would include the production of coagulase, the presence of the type A polysaccharide of Julianelle, usually liquefaction of gelatin and fermentation of lactose, mannitol and potential pathogenicity for man.

Bacteriology and morbid anatomy

Pneumococcal endocarditis.—R. W. Luxton and G. S. Smith analyse twenty cases of fatal pneumococcal endocarditis and review the recent work on this infection, the last survey of which in Great Britain appeared in 1906 by Lord Horder. The author of the present paper found that the disease is almost always associated with pneumonia, and is very prone to give rise to generalized pneumococcal infection with meningitis and empyema. The most common pneumococcus found to be responsible was type I; it occurs in from 5 to 15 per cent of all cases of pneumonia and is the most common type in pneumococcal endocarditis in middle life. The left side of the heart is attacked oftener than the right, and the aortic valve segments are oftener involved than are those of the mitral valve. The lesions of the cardiac valves are so characteristic as to be almost diagnostic. Previous damage to the valves appears to dispose to pneumococcal endocarditis, but syphilitic aortitis is seldom a precursor. The vegetations are usually larger than are those in endocarditis due to *Streptococcus viridans*, but the size varies with the duration of the infection; they may be single, polypoid, or yellowish green, with a smooth surface. The clinical features are fairly characteristic; the spleen is rarely palpable, the fingers are seldom clubbed because of the short duration of the disease and the heart signs are not always duly appreciated. Signs of pericarditis during or after pneumonia should arouse suspicion of the disease. Eight of the twenty patients had an empyema, and it is suggested that any factor delaying the diagnosis and delaying early drainage of an empyema may favour the onset of pneumococcal endocarditis. Type-specific serum and sulphapyridine may have some symptomatic effect but cannot bring about a cure.

Treatment

Bacteriostatic action of sulphonamide compounds.—E. S. Orgain and Mary A. Poston report a comparison of the inhibitory effects *in vitro* and the bacteriostatic activity observed in patients with bacterial endocarditis treated by one or more of seven sulphonamide drugs. The data bearing on the correlation of inhibitory action *in vitro* and *in vivo* are brought forward, and it is concluded that there is a certain degree of correlation between the inhibitory action *in vitro* of the sulphonamide drugs and their clinical bacteriostatic activity. The importance of preliminary experiments *in vitro* to determine the most effective drug and its possible clinical level of inhibitory action is emphasized. Although sterilization or inhibition of growth may result in a lower concentration of the drug in the body than in the test-tube, the converse is not true.

Horder, Lord (1906) *Med.-chir. Trans.*, **89**, 333.

Luxton, R. W., and Smith, G. S. (1943) *Quart. J. Med. N.S.*, **12**, 61.

Orgain, E. S., and Poston, Mary A. (1942) *Arch. intern. Med.*, **70**, 777.

Penfold, J. B. (1943) *J. Path. Bact.*, **55**, 183.

HEART DISEASES: MITRAL VALVE DISEASES

See also B.E.M.P., Vol. VI, p. 309; and Cumulative Supplement, Key Nos. 647-651.

Mitral stenosis

Clinical picture

Relative mitral stenosis.—C. Bramwell suggests the term, relative mitral stenosis, to describe the effects of increased rate of blood flow through a normal mitral orifice. Duplication of the second heart sound at the apex is apt to be regarded as evidence of an organic mitral lesion; in the author's opinion this sign is physiological. It is best heard with the subject lying on his

left side, probably because the blood stream is then flowing horizontally and not directly against gravity as it does when the subject lies on his back, and thus the blood flow from auricle to ventricle is accelerated. The duplicated second sound is much commoner in young subjects than it is in older persons; thus in a series of 835 recruits 19 per cent manifested this sign but it was present in 43 per cent of those under twenty, and in only 10 per cent of those over that age. Most of the young men concerned appeared to be perfectly fit; 70 per cent were put in grade I. No significant difference of pulse rate or of systolic pressure existed between those with and those without the duplicated second sound. Only a few of the electrocardiograms showed right axis deviation but in most cases the X-ray film suggested that the pulmonary arc was more prominent than usual in the men with reduplication of the second sound, the heart conforming to the childish contour. The duplicated second sound was generally associated with an apical systolic murmur or with an impure first sound; this murmur is possibly due to a 'safety-valve mitral incompetence' associated with overfilling of the ventricle. A presystolic murmur has been heard in the hearts of normal athletes, and a similar explanation, namely increased rate of flow through a normal mitral orifice, probably applies. A similar modification of the first heart sound is apt to occur in any excitable overacting heart, for example when thyrotoxicosis is present.

Bramwell, C. (1943) *Brit. Heart J.*, 5, 24

HEART DISEASES: AORTIC VALVE DISEASES

See also B.E.M.P., Vol. VI, p. 329.

Morbid anatomy and bacteriology

Malignant endocarditis

Subacute monilial endocarditis —J. G. Pasternack describes as a new clinical and pathological entity, subacute monilial endocarditis, in a man aged forty-five years. At the necropsy were seen vegetations which almost occluded the aortic orifice and were implanted on a sclerotic and calcified obsolete lesion of the valve cusps. The spleen weighed 1,080 grammes, was much enlarged and softened and showed extensive thrombosis and thrombocytosis in the pulp. During life the blood provided organisms which were compatible with a diagnosis of *Candida* (*Monilia*) *parakrusei*. Examination of the cardiac vegetations did not show any micro-organism other than monilia. The author refers to six cases of subacute monilial endocarditis, five being due to *C. parakrusei* and occurring in drug addicts; the patient concerned in the remaining case was infected with *C. guillermoidi*.

Pasternack, J. G. (1942) *Amer. J. Clin. Path.*, 12, 496.

HEART DISEASES: HEART FAILURE

See also B.E.M.P., Vol. VI, p. 368; and Cumulative Supplement, Key No. 659

Physiology: the cardiac reserve

Factors which reduce the cardiac reserve

Hypertension causing cardiac hypertrophy and dilatation —F. A. Willis of the Mayo Clinic agrees with the view that the primary mechanical factor in the production of hypertension is constriction of the arteriolar bed of the body (vasospasm). This change may at first be transient but later may become permanent as obliterative lesions occur in the arterioles. Thus with the resulting changes in the arterial blood pressure and the increase in the peripheral arterial resistance, an added load is imposed on the left ventricle of the heart which responds by hypertrophy in the same way as other muscles do. The heart is able within certain limits to respond to increased work; the limit of response is what is commonly known as the cardiac reserve. The energy output of the heart depends on the diastolic length of the muscular fibres, and when dilatation occurs under a constant load it does so only because the ventricle is incapable of ejecting as much blood at each beat as is delivered to it. Then residual blood accumulates in the left ventricle and an increased load is imposed on the left auricle which, in turn, increases the pressure within the pulmonary circulation; in this way the beginning of a vicious cycle is started. Increased pressure in the pulmonary circulation is reflected on the right side of the heart, the dilatation of which, when it ultimately occurs, results in incompetence of the tricuspid valve. Other important mechanisms share in the vicious cycle eventuating in congestive heart failure.

Treatment

Drugs

Single dose digitalization.—Single dose digitalization has many practical advantages over the divided dose method, and digitoxin, on account of the rapidity and regularity of its absorption, is—according to H. Gold, N. T. Kwit, McK. Cattell and Janet Travell—the preparation of choice. They have studied its effects in a series of 213 patients with varying degrees of heart failure, all of whom had not taken digitalis for three weeks previously. Each received a single oral dose of 1.26 milligram, which is the average total digitalizing dose. Toxic symptoms followed in 4.6 per cent, but in no case were they serious, consisting only of gastro-intestinal irritation. When the total digitalizing dose was given as a single dose of digitalis leaf or of tincture, either nausea or nausea and vomiting occurred in 19.3 per cent; some other

constituent or impurity is probably to blame. The use of digitoxin by single dose administration offers a means of bringing a patient under the influence of digitalis within a few hours.

Gold, H., Kwit, N. T., Cattell, McK., and Travell, Janet (1942) *J. Amer. med.*

Ass., **119**, 928.

Willius, F. A. (1942) *Proc. Mayo Clin.*, **17**, 606.

HEREDITY AND CONSTITUTION

See also B.E.M.P., Vol. VI, p. 452.

Constitution

Minor disabilities

Clinical types and treatment.—W. C. Alvarez discusses the problem of the patient who is always 'under the weather' yet does not present any sign of organic disease. Such people tend to go from one doctor to another, and may be treated for one small physical abnormality after another without relief, with consequent waste of their time and money. The condition appears to be due mainly to mental causes; although physical inferiority may play a part, there is a strong hereditary tendency. The patients are of several types, such as the asthenic person who cannot stand much work or loss of rest, the person with low resistance to infection, and so forth. The diagnosis can be made after talking to the patient, and a correct diagnosis is of the greatest importance since it may save him unnecessary medical and possibly surgical treatment; even if such a subject develops some organic disease, for example, duodenal ulcer, no treatment, however successful as regards the local lesion, will succeed in giving him normal health. The patient needs to be taught to accept the situation and make the best use of his limited capacity.

Alvarez, W. C. (1942) *J. Amer. med. Ass.*, **119**, 780.

HISTOPLASMOSIS

See also B.E.M.P., Vol. VI, p. 520

Morbid anatomy

Microscopical

Clinical course and histological observations—W. McK German, S. Ashmun and C. E. Dille report a case, fatal on the twentieth day of illness, of anaemia and loss of appetite in a male, aged sixteen weeks. The infant was admitted to hospital with a temperature of 103° F., and with hepatic and splenic enlargement and anaemia, early leucopenia gave place to terminal leucocytosis due to pneumonia. Temporary improvement occurred after blood transfusion. Necropsy showed advanced generalized reticulo-endotheliosis of the viscera, spleen, liver, kidneys and lymphatic glands, but not any true granulomas. The heart contained focal accumulations of monocytes. The thymus gland was very small with pronounced atrophy of the lymphoid elements and with gross parasitic involvement. The histological appearances justified the diagnosis of histoplasmosis.

German, W. McK., Ashmun, S., and Dille, C. E. (1943) *Amer. J. Clin. Path.*, **13**, 12.

HODGKIN'S DISEASE

See also B.E.M.P., Vol. VI, p. 523, and Cumulative Supplement, Key No. 691.

Clinical picture

Conspicuous lesions on the skin

Atypical microscopical characters.—A case of lymphogranulomatosis with the most conspicuous lesions in the skin is reported by H. A. Reimann, W. P. Havens and P. A. Herbut. A man aged forty-five complained in March, 1939 of tiring more quickly than usual. In April, several red spots appeared on the extensor surface of the right arm near the elbow. They were about 5 millimetres in diameter, they itched and at times were painful enough to keep him awake at night. After several days they faded, leaving pigmented areas. The man continued at work but lost weight, strength and appetite. Three weeks later similar but more numerous and less painful nodules appeared upon the abdomen and chest. Most of these subsided after several months, leaving brownish spots. Some of them ulcerated and became covered with dark crusts and then healed slowly. In May the patient was admitted to hospital with jaundice and while there developed pitting oedema of the legs and trunk which rose as high as the xiphisternum; there was also remittent fever, the temperature reaching 103° F. on several occasions. The lymphatic glands in the axillae and groins were palpable. An excised lesion from the skin was examined by a dermatologist who suggested a diagnosis of chronic panniculitis (Weber-Christian syndrome). Blood examination in June showed 75 per cent haemoglobin, 4,000,000 erythrocytes and 6,000 leucocytes per cubic millimetre, and an erythrocyte sedimentation rate of 10. An X-ray examination of the chest showed increased density of the tracheo-bronchial shadows and broadening of the peripheral bronchi, suggestive of an infiltrative process. The patient's tonsils were excised in the hope that they were at the root of the trouble, and he was given sulphapyridine, without effect. After his return home he improved slightly but remained febrile. Several weeks later high fever recurred and he re-entered the hospital on September the 1st. The skin eruption reappeared. The spleen was now

palpable and an X-ray film of the chest showed changes resembling those seen in pulmonary Hodgkin's disease. The patient was observed for the next nineteen months; he gradually became worse, and died in May, 1941, about two years after the onset of the illness. At necropsy the chief finding was enlargement and coalescence of the lymphatic glands in the mesentery, at the hilum of the liver and along the aorta. Scattered tumour masses were present in the lungs, kidneys and liver. Microscopically the lesions showed the typical appearances of Hodgkin's disease; sections of the cutaneous nodules were atypical, as before.

Bone lesions in Hodgkin's disease and in lymphosarcoma

Incidence and clinical signs.—Bone involvement, excluding the terminal bone marrow involvement which occurs in almost all cases of Hodgkin's disease, is an important and not uncommon complication of Hodgkin's disease and of lymphosarcoma. J. O. Vieta, H. L. Friedell and L. F. Craver, in a study of 257 cases of Hodgkin's disease and of 213 cases of lymphosarcoma, state that X-ray evidence of bone involvement was found in 14.8 per cent of the former and in 7 per cent of the latter. These figures are almost certainly too low, for the reasons given as follows. Radiological examination is often inadequate or is omitted altogether, and only comparatively advanced bony changes are shown by X-ray examination. It is probable that a more accurate idea of the incidence could be obtained by systematic radiographical examination in lymphosarcoma than in Hodgkin's disease, because the destructive process appears to be much more rapid in the former disease. Necropsy findings in forty-seven cases of Hodgkin's disease and in fifty-four cases of lymphosarcoma included osseous lesions in 49 per cent of the former and in 29 per cent of the latter. These figures again are probably too low because examination was limited to easily accessible bones. The symptoms and signs of skeletal involvement include localized pain and tenderness, palpable swelling and neurological abnormalities (when the spine is involved). The general constitutional changes do not differ in any important respect from those observed in cases in which bony lesions cannot be demonstrated. Blood changes due to lesions of the haemopoietic system appear to be more common in Hodgkin's disease than in lymphosarcoma, owing to the fact that the number of osseous lesions tends to be greater in Hodgkin's disease. Abnormally high serum phosphatase values are found in some cases of bony involvement. In the writers' series this sign was present in nine of eighteen patients with Hodgkin's disease of bone in whom determinations were made, and in two of five patients with lymphosarcoma of bone. Elevated phosphatase values reflect any abnormal osteoblastic activity and are therefore not found in connexion with purely destructive lesions of bone. Involvement of bone in Hodgkin's disease or in lymphosarcoma may occur either by extension from adjacent lymphatic glands or by the haematogenous route. Necropsy findings in the writers' series of cases suggested that, when haematogenous spread takes place, an embolus first lodges in the marrow and later invades the bone cortex. The regions in which red bone marrow chiefly occurs, that is the vertebrae, ribs, pelvis, femora, were those most often affected in Hodgkin's disease and in lymphosarcoma, as they are in cancer. The general impression that osseous involvement is a late event is not confirmed. Of forty-four cases of Hodgkin's disease—including twenty-five in the present series—in which the necessary data were available, 37 per cent showed osseous involvement in the first half of the illness. In lymphosarcoma, on the other hand, bone lesions occurred during the first half of the illness in only 22 per cent of twenty-seven patients and in the final third of the course in 63 per cent. Radiotherapy usually brings considerable relief of symptoms.

Hodgkin's disease of the breast

Histological observations on mitoses.—S. Wray records a case in a woman, aged twenty-seven, of acute Hodgkin's disease of the left breast, with enlarged glands on both sides of the body and in the axillae and inguinal regions. A prominent histological feature was the presence of mitoses, some of them being multipolar and suggesting malignant disease. The author refers to five previously recorded cases; of three of these the case reports by H. Kückens, by R. Pettrignani and by J. E. Gendreau and G. Pinsonneault are given. In the remaining two recorded cases data were not available.

Hodgkin's disease in pregnancy

Clinical course after X-ray irradiation.—M. G. Spiesman and H. I. Rubenstein report the following case of Hodgkin's disease. A married woman, aged twenty-four, was first seen in November, 1931, complaining of a dry cough of four weeks' duration. On examination she was somewhat obese and had mild fever; the tonsils were small and did not appear to be infected and the chest findings were negative. She was not seen again until July, 1932, when she was again complaining of cough. Examination showed that the temperature was 100.8° F., and there was a small mass in the right supraclavicular region and enlarged lymphatic glands were present in both axillae. The leucocyte count was 24,900; the differential count showed neutrophils 80 per cent, small lymphocytes 16, large lymphocytes 1, eosinophils 2. The erythrocyte count was 4,010,000. Mantoux, Wassermann and Kahn tests gave negative results, as did also agglutination tests for undulant fever. Stereoscopic X-ray films of the chest showed moderate fibrosis in both lung fields and a mass, presumably an enlarged lymphatic gland, at the right hilum. Biopsy of the cervical mass showed an early stage of Hodgkin's disease. Deep X-ray therapy was given to the neck, sternum, chest and axillae, and the enlargement of the lymphatic glands disappeared. In 1933 the woman became pregnant and in 1934 gave birth to a healthy baby. During her pregnancy permanent solid

oedema of the left arm appeared, and during the three months after delivery oliguria developed, with pain in the abdomen and left lumbar region, and with progressive oedema of the legs. In August, 1934 indirect pyelography demonstrated a non-functioning left kidney. An exploratory operation was carried out, and a mass of lymphatic glands weighing several pounds was found compressing the left kidney and ureter and extending down into the pelvis. Biopsy of the mass showed a more advanced stage of Hodgkin's lymphogranuloma. X-ray therapy was again given and resulted in clinical improvement and gain in weight. Recurrent enlargement of different groups of lymphatic glands responded similarly to X-ray treatment, and the patient remained in fair health for eight years. During the last year progressive signs of rectal obstruction developed, including alternating constipation and diarrhoea with passage of blood and mucus. In 1939, rectal examination demonstrated a firm infiltrated constricting ring about four inches above the anus. X-ray treatment produced very little symptomatic improvement. Biopsy specimens showed infiltration of the rectal wall by lymphogranulomatous tissue. A barium sulphate enema showed constrictions in the rectal and sigmoid regions. Further X-ray therapy was given. The patient improved for a few weeks but then became progressively worse and died with terminal bronchial congestion in January, 1940. A necropsy could not be performed. The authors point out that gastro-intestinal Hodgkin's disease may be the only lesion or it may be part of a disseminated process. The lymphogranulomatous infiltration usually spreads into the bowel from the mesenteric lymphatic glands either by continuity or by retrograde lymphatic transport. Clinically such cases fall into two groups. The inflammatory variety simulates tuberculous enteritis with abdominal pain, diarrhoea and passage of blood and mucus; the obstructive type simulates carcinoma. Differential diagnosis of rectal Hodgkin's disease is made by biopsy.

Treatment

Radiotherapy

Technique of treatment.—A. U. Desjardins discusses the radiotherapeutic problems presented by Hodgkin's disease and by lymphosarcoma. Treatment must be arranged so as to deal as effectively as possible with the lesions responsible for the symptoms. (1) For cervical lymphadenopathy, if it is at all extensive, each side of the neck must be divided into two or more fields, beams of rays being directed so as to converge on the enlarged lymphatic nodes from both sides of a line extending from the lobe of the ear to about the middle of the clavicle. When the nasopharynx, pharynx or tonsil is involved treatment must take into account the thickness of the tissues of the neck and face. If the process has extended to one or more of the accessory sinuses one or two additional anterior fields may be necessary. (2) Mediastinal lymphadenopathy is best dealt with through two anterior and two corresponding posterior fields. The dose of the irradiation must be sufficiently large and must be administered in a sufficiently short space of time. When the principal involvement is high in the mediastinum the lower half of the neck should also be irradiated from each side by two converging beams. (3) Axillary lymphadenopathy needs attention only when causing symptoms. In mild cases one beam directed upwards and inwards through a single field may suffice, but in more advanced cases two to five convergent beams should be used. (4) Abdominal lymphadenopathy requires different arrangement of fields according to the position of the lymphatic glands chiefly affected. Irradiation of the pelvic organs should not be carried out in women under forty years if it is not absolutely necessary, because an artificial menopause adds to the patient's discomforts. Closer watch than usual must be kept on the leucocyte count when the abdomen is irradiated. The author's best results have been obtained by the use of 140-kilovolt rays in a dosage of 550 to 600 r to each field in succession. The number of days of treatment required depends upon the extent of the disease and upon the tolerance of the patient, but should be as small as possible; from ten to sixteen days is suggested as the time to be taken for irradiation of most of the lymphatic glands of the body. Excessive quantitative dosage may lead to increasing radio-resistance. Special problems are presented by infiltration of the skin, subcutaneous tissues, abdominal organs, rectum, ureters or kidneys, suprarenal glands, orbits, bronchi and meninges. Infiltration of these is always a late manifestation, and radiotherapy can be expected to give only temporary although sometimes very considerable relief.

EDITORIAL COMMENTARY—Recent Observations in Hodgkin's Disease

Hodgkin, in 1832, first described a syndrome consisting of enlargement of superficial lymphatic glands, enlargement of the liver and spleen, with anaemia, causing cachexia and a fatal termination. Of the seven original cases, H. Fox showed that only three were cases of what is now regarded as Hodgkin's disease, but it is a tribute to Hodgkin's diagnostic powers that, even at the present time, less than 50 per cent of cases diagnosed on clinical grounds as Hodgkin's disease or lymphadenoma are subsequently confirmed as such. Diseases commonly mistaken for this condition are the endothelial form of glandular tuberculosis in young people and lymphosarcoma in older people; less often endothelial sarcoma, reticulosarcoma, 'reactive follicular hyperplasia', and leukaemia cause difficulty in diagnosis.

Clinically, the disease usually starts as a painless enlargement of lymphatic glands in one or more of the triangles of the neck; in this type the disease remains localized to the neck for a time, and has led surgeons to remove the glands in a hope of eradicating the disease, a procedure which has received recent support from C. Baker and W. N. Mann. Sooner or later other glands are involved, in a spread which seems to occur via the lymphatic vessels

and often to proceed in a centripetal manner to the lower cervical glands, to the axillary and mediastinal glands, and later still to the abdominal and inguinal groups. A second type starts in the chest, with enlargement of the mediastinal glands which produces the signs of a mediastinal tumour, and the disease may spread in the peribronchial structures to produce a characteristic radiological picture: enlargement of the supraclavicular, subclavicular or axillary lymphatic glands occurs early in this form, and is sometimes the earliest presenting symptom, but it is comparatively rare to see distant glands involved, and therefore the upper cervical and inguinal glands rarely become palpable, and the spleen and liver seldom enlarge to the extent associated with the first type above. These different glands at first produce local symptoms, but sooner or later toxæmic symptoms arise with pyrexia, sweating which may be profuse, tachycardia, loss of weight and, later still, anaemia. There is little doubt that this stage represents a spread of the disease by the blood stream, and it is interesting to conjecture whether or not the Pel-Ebstein temperature chart may not represent a periodic blood-borne spread at regular intervals, thereby bearing a resemblance to the relapsing fevers; a relapse is repeatedly heralded in some by an obvious rigor. This phenomenon of blood-borne dissemination in the later stages has recently received interesting confirmation from a study of the deposits met in bone marrow and in the bones themselves. The almost constant symptom of intractable headache met in this stage of the disease is clearly related to the involvement of bone and may be much ameliorated by X-ray therapy, even when radiographical changes cannot be demonstrated. In spite of the widespread bone involvement, collapse of a vertebra is hardly ever seen.

In the earlier stages, diagnosis can be made with certainty only after biopsy of a lymphatic gland has shown characteristic histological features of the disease, of which the most important are the widespread fine fibrosis, the presence of Dorothy Reed giant cells, of polymorphonuclear cells and sometimes of eosinophils. These histological changes are more advanced in the first lymphatic glands to be involved, a point to be borne in mind when selecting a gland for biopsy. Gordon's test still stands the test of time and, whatever may be the final interpretation of it, there is no doubt that the intracerebral inoculation of gland suspension in rabbits or guinea-pigs, with the production of an encephalitis, gives an early and dependable diagnosis of the disease in many cases in which this is not possible otherwise. The changes in the leucocyte count of the blood are also remarkably uniform. The total leucocyte count may be low, normal or high (even to 30,000) but the relative polymorph count soon reaches at least 70 per cent and often approximates to 90 per cent of the total cells. Another characteristic finding is a high erythrocyte sedimentation rate; in the very earliest stages a value within normal limits may be found, but soon the value rises and very high figures may be recorded even when the patient is not noticeably anaemic or particularly ill, there is undoubtedly a close connexion between the erythrocyte sedimentation rate and the clinical condition of the patient. On the whole, present-day evidence supports the view that the granulomatous lesions are the result of an infective agent, and in this connexion the frequent occurrence of herpes zoster and sometimes of a rash resembling generalized vaccinia is not without significance.—F. C. WARNER.

Baker, C., and Mann, W. N. (1939) *Guy's Hosp. Rep.*, **89**, 83.

Desjardins, A. U. (1942) *Radiology*, **39**, 16

Fox, H. (1936) *Guy's Hosp. Rep.*, **86**, 11.

Gendreau, J. E., and Pinsonneault, G. (1939) *Un. med. Can.*, **68**, 161.

Kuckens, H. (1928) *Beitr. med. Wschr.*, **66**, 1220

Petrignani, R. (1930) *Ann. Anat. path. méd.-chir.*, **8**, 360

Reimann, H. A., Havens, W. P., and Herbut, P. A. (1942) *Arch. intern. Med.*, **70**, 434.

Spiesman, M. G., and Rubenstein, H. I. (1942) *Ann. intern. Med.*, **17**, 349.

Vieta, J. O., Friedell, H. L., and Craver, L. F. (1942) *Radiology*, **39**, 1.

Wray, S. (1943) *J. Path. Bact.*, **55**, 75.

HYPOGLYCAEMIA AND HYPERINSULINISM

See also B.E.M.P., Vol. VII, p. 42; and Cumulative Supplement, Key No. 712.

Morbid anatomy

Pancreatic lesions

Carcinoma of the pancreas.—L. M. Gray reports the case of an obese woman, aged forty-eight, with severe hypoglycaemia, who underwent excision of a primary carcinoma of the tail of the pancreas, the growth measuring 1.8 × 1.3 × 1.3 centimetres. At necropsy the liver, weighing 1,510 grammes, contained numerous firm white glistening nodules, from 2 to 3 centimetres in diameter, which in many instances showed hard yellow centres. Metastases were also present, in the peripancreatic, peri-aortic and mediastinal lymphatic glands, in the spine, lungs and pleurae, and in one adrenal gland. At least a third of the liver was occupied by growth. The patient survived the operation for nearly six weeks. Microscopically the cells in the hepatic nodules varied considerably and resembled islet cells on a large scale. The cell which was most often present was tall, columnar and generally acidophil; in other areas, tall regular columnar cells formed tubes; a third type of cell was polyhedral. Although many cells resembled large islet cells, they failed to take any of the special stains for alpha and beta cells.

The central part of the anterior lobe of the pituitary gland was composed of massed acidophil cells. Analysis of cases of primary carcinomas of islet cells shows how remarkably rare are metastases; Gray has collected nine such cases, including his own.

Changes in central nervous system

Brain lesions in fatal hypoglycaemia.—R. D. Lawrence, A. Meyer and S. Nevin report their observations on six fatal cases of hypoglycaemia and use them as a basis for a review of the whole subject. In the above six cases the intensity and the duration of the hypoglycaemia are not known accurately. Further, in some of the cases previous attacks of hypoglycaemia with convulsions had occurred and it is possible that they had produced permanent morbid lesions. Although in all cases the nerve damage appeared to be sufficient to be the direct or indirect cause of death, it is probable that in two cases cardiac failure was a contributing factor. The lesions were similar in all the cases, differing only in the intensity and stage of the process. Widespread degeneration and necrosis of nerve cells were found, with corresponding microglial and macroglial proliferation, and with homogenizing and gross nerve cell changes. The cerebral cortex, the caudate nucleus and putamen were affected most; the cerebellum was less affected, and the lesions in the remaining centres of the brain stem were slight. The pathogenesis is discussed in relation to biochemical alterations occurring in hypoglycaemia; the latter are compared with similar changes occurring in anoxia. The main cause is failure of vital oxidative processes from the lack of the substrate glucose, probably reinforced by subsequent vasomotor disturbances. The relative part played by the chemical and circulatory factors cannot be assessed and probably varies from case to case, but the primary factor seems to be chemical and allied to anoxia.

Treatment

Spontaneous hypoglycaemia

Treatment measures summarized.—Measures to deal with prolonged hypoglycaemia are described by H. Pullar-Strecker. Failure to wake after the administration of adequate amounts of intravenous glucose, of which up to 250 cubic centimetres of 33 per cent solution may be required, means that the coma has passed from the hypoglycaemic to the post-hypoglycaemic stage, in which the blood sugar is normal or raised and unconsciousness persists because of cellular changes occurring during hypoglycaemia. Treatment includes inhalation of oxygen with 5 per cent carbon dioxide, intravenous injections of vitamin B, adrenal cortical hormone and calcium chloride; saline infusion; gastric lavage; withdrawal of as much cerebrospinal fluid as possible; and blood transfusion if all else fails.

Gray, L. M. (1942) *Amer. J. Path.*, **18**, 633.

Lawrence, R. D., Meyer, A., and Nevin, S. (1942) *Quart. J. Med. N.S.*, **11**, 181.

Pullar-Strecker, H. (1942) *Brit. med. J.*, **2**, 350.

IMPETIGO

See also B.E.M.P., Vol. VII, p. 81; and Cumulative Supplement, Key Nos. 734 and 735.

Acute impetigo

Actiology

Discussion of causes and treatment.—J. W. Biggs and G. A. Hodgson have investigated the bacteriology of 130 cases of impetigo occurring in men (96 per cent) and women (4 per cent) in the Forces. The cases were classified as mild, medium or severe according to the extent of the disease. In every case cultures (one or two) were made before treatment was begun and in many cases further cultures were made during treatment. From 230 lesions examined eighty-five strains of haemolytic streptococci were isolated. All but five of these were tested with the following results: group A, sixty-nine; group B, none; group C, three; not A, B or C, eight. Thus, assuming that the remaining five strains belonged to group A, *Streptococcus pyogenes* was present in seventy-four instances, other haemolytic streptococci in eleven. Staphylococci were found in 216 lesions. Of these 216 strains 173 were coagulose-positive and should be classed as *Staphylococcus pyogenes*. Other organisms occurred infrequently. Cultures could be obtained in the vesicular stage from only ten patients. Of seventeen vesicles examined all yielded pure cultures of *Staph. pyogenes*. There were not any differences to be observed between lesions which yielded *Strep. pyogenes* and those which did not. It is believed that most if not all cases of impetigo are primarily due to *Staphylococcus pyogenes*. H. L. Sheehan and A. G. Fergusson in a study of ninety-seven soldiers found that *Staphylococcus aureus* was present in nearly every case and that haemolytic streptococci were met with more rarely and only in the later stages, after the initial blister had become crusted. These authors divided the affected skin into three or four areas, each of which was treated by a different method. The most effective of the preparations used was found to be a paste consisting of copper sulphate 3 grains, zinc sulphate 2 grains, precipitated sulphur 5 grains, sulphathiazole ten tablets (powdered), zinc oxide half an ounce, starch powder half an ounce and soft paraffin 1 ounce. This paste used in a series of twenty-five cases cured most within five days and all within eight days. In a Leading Article commenting on these two papers it is pointed out that they furnish fairly conclusive proof of the staphylococcal origin of impetigo in adults and appear to be at variance with the evidence in favour of a primary streptococcal infection. Some authorities hold that two forms of impetigo exist: the streptococcal variety,

commoner in young children and having its maximum incidence in the autumn, and the staphylococcal type, having its maximum incidence in summer.

Treatment

General and local treatment.—R. T. Brain emphasizes the difficulty of distinguishing clinically between staphylococcal and streptococcal lesions in impetigo contagiosa. Streptococci have often been found in pure culture even in bullous impetigo, many cases of which respond dramatically to sulphonamides. Of the clinical varieties of lesion the scabbed sore is the most common. Bullous lesions are evidence of a more virulent infection and the spread is usually rapid. After rupture of the bullae the edges may remain red and may extend as a circinate lesion resembling tinea but progressing more rapidly. Ulcerative lesions known as ecthyma develop in rare cases, and leave scars. Pale scaly lesions characterize the variety called impetigo pityroides. Impetigo often produces chronic septic fissures at the angles of the mouth and septic intertrigo in skin folds, particularly behind the ears. In some cases, owing either to the virulence of the infection or to the irritative effect of treatment, a rapidly spreading pus-coccal dermatitis supervenes. Weeping dermatitis is often loosely called eczema, but true eczema may occur as a result of sensitization of the skin either by the infection or by some therapeutic application. In most cases of impetigo general treatment is of minor importance, but in the exceptional case a virulent organism or lack of resistance on the part of the patient produces a rapidly spreading infection, the lesions of which are deeply coloured and have an erysipelatous flare around them. In such cases general treatment is vital, and treatment by sulphanilamide, 1 gramme three or four times a day for a week, is usually followed by rapid improvement. As a safeguard against toxic symptoms, and because war-time diets are low in vitamin C, the giving of ascorbic acid in doses of 50 milligrams two or three times a day is advisable. In obstinate chronic cases of impetigo it is worth while to try vitamin C alone. Ultra-violet light therapy may be helpful. Phenobarbitone is recommended for nervous subjects who frustrate local treatment by picking at the sores even during sleep. Local treatment depends upon the conditions. A moist skin favours the spread of infection and water or grease should, therefore, be avoided in general. To prevent spreading of impetigo on the face by the pillow at night a useful measure is to soak a clean handkerchief in liquor hydrargyri perchloridi, dry it, pin it to the pillow and lightly powder it with talc. The nails should be kept short, scrubbed and treated with an antiseptic to minimize the risk of reinfection by scratching. Scabs and exudate should be cleaned away by means of hot compresses of 2 per cent sodium sulphate, this being followed by bathing with the same solution or with 1 per cent sodium bicarbonate or normal saline. Treatment, having cleaned the skin, must now aim at drying it, either by such means as radiant heat, ultra-violet or infra-red light, or with powders and drying lotions. Sulphanilamide powder is effective but starch should be avoided. Gentian violet solution, 2 per cent, is excellent, and calamine lotion is useful in mild cases. Creams and pastes should be tried if the skin becomes too dry or if eczema occurs. Ointments are, usually, harmful rather than helpful.

Local use of sulphonamides.—The favourable reports on the use of sulphonamide derivatives in ointment form for infections of the skin have led J. L. Miller to try it on forty-five patients with impetigo contagiosa. The preparations used were sulphanilamide, sulphathiazole, sodium sulphathiazole and sulphadiazine. They were incorporated in one or other of two different bases, consisting essentially of emulsions of water in oil. The base most frequently used contained diethanolamine oleate, white wax, liquid petrolatum and distilled water. The drugs were in a suspended state and in solution to about the degree of their solubility in water, namely 0.8 per cent for sulphanilamide and 0.1 per cent for sulphathiazole. Cultures were made from the lesions before and after treatment in a number of cases. A close correlation was observed between the number of colonies and the clinical condition, relapses being associated with a rising count. Negative plates were common after one week's treatment with the ointment, which was applied twice daily after previous application of hot boric acid compresses. All except one of the patients were cured in three to ten days, the average being six days; such an average time is considerably shorter than that reported for accepted measures of treatment. Twenty-one patients had used ammoniated mercury or gentian violet previously but without benefit. In most cases sulphanilamide or sulphathiazole was used, with equally good results; a few patients received sulphadiazine ointment, but the results were not so striking. The only reaction noted occurred in a patient treated with 50 per cent sulphathiazole ointment for ten days. He developed a generalized vesiculo-pustular dermatitis. The condition began to improve two days after the ointment was discontinued and cleared up completely in three weeks. A patch test with the ointment base gave a negative result. Five per cent ointments are recommended for routine use, since they are as efficacious as and are less liable to produce reactions than is a more highly concentrated ointment. The local use of sulphonamide derivatives is advocated by A. J. Steigman who finds that the best results are obtained by sulphathiazole or sulphadiazine. The average length of time required for cure with sulphathiazole ointment is four to five days. Local application not only eliminates the disadvantages of systemic chemotherapy but is much more economical, since the amount of sulphonamide which one patient would need to take by mouth makes enough 5 per cent ointment to treat many patients locally.

Action of strong tincture of iron perchloride.—C. S. Smith has treated a large number of cases of impetigo contagiosa by application of liquor ferri perchloridi fortis without previous

removal of the scabs. The results have been excellent, the spread of the infection has ceased and the period of infectivity has been considerably shortened. The solution has an antiseptic and astringent action. The treatment is simple and cheap, and avoids the use of fats, but it is painful and for young children gentian violet, 2 per cent, has been substituted. Treatment with the latter is more prolonged.

Impetigo in the Forces

Lessons from the Navy and Army.—The necessity for economy in war-time is emphasized by R. W. Carslaw, who has treated over a hundred cases of impetigo among naval men in the home climate and in the Tropics. In the home climate the treatment successfully used was sulphanilamide ointment and afterwards a brilliant-green stearate paste. In the Tropics the paste was not stiff enough and the sulphanilamide preparation was contra-indicated on account of its ointment base. Here the treatment used was swabbing with lotio hydrargyri perchloridi, 1 in 1,500, followed by application of lotio calaminæ. This treatment was carried out twice a day in twenty-seven cases without a failure. Firm dry crusts were formed which, on separating, left a healed surface. J. T. Ingram, from his experience with the B.E.F. in France in 1939–40, lays down the guiding principle in treating impetigo that ointments are to be avoided and the skin kept dry. Various preparations were used, including solutions of the dyes, cau d'Alibour followed by dusting powder or calamine, ammoniated mercury 2 per cent in Lassar's paste and starch poultices and potassium permanganate compresses; results were generally good. Many medical officers used sulphanilamide or sulphapyridine externally or internally. The results, although good, were not so remarkable as to convince Ingram of the desirability of making this the routine treatment, in view of the danger of poisoning or of sensitizing the patient to a drug which he might later need urgently for some more serious condition.

EDITORIAL COMMENTARY—Impetigo: The Main Advances Reviewed

The above abstracts show the interest taken during the past year in the treatment of impetigo. There are three reasons for this—first the apparent increase in the incidence of the disease, secondly the difficulty experienced in its management, and lastly the wide use of the sulphonamide drugs in the treatment. Reports on the value of the sulphonamides have been favourable, although Brain (1942) states that these drugs are rarely necessary in impetigo. Routine treatment by oral administration has been suggested by B. E. Schlesinger and N. H. Martin (1942) but this is further than most dermatologists would go. Impetigo contagiosa is not a notifiable disease and, therefore, correct figures cannot be given concerning its incidence. However, it is reasonable to believe that the incidence of impetigo has increased, for there is a correlation between it and personal uncleanness. With the crowding of civilians in air-raid shelters and public vehicles, and of troops everywhere, favourable conditions for the spread of cutaneous bacterial infection must obtain.

The possibility of a vitamin deficiency as a causal factor is often raised, usually by the patient, but is probably of little importance. Brain suggests, however, that a vitamin C deficiency may be worth considering as a contributory factor in chronic impetigo.

Pediculosis capitis and pediculosis corporis greatly increased among the civil population after the concentrated air raid period, and brought an increase in impetigo of the head, neck and body. Scabies is still prevalent and should always be remembered as a possible cause of chronic impetigo. The impetigo involves the sites of election of the mite, that is the wrists, fingers, insteps and buttocks.

To be successful, the treatment of impetigo must be based on a knowledge of its aetiology, and the appearances at all stages of activity and of healing. The physician should be able to recognize overtreated impetigo lesions, and the signs of intolerance to any medicament used. Such intolerance is shown by redness and slight oedema of the skin, irregular vesication and, later, weeping and crusting, in some instances the disease may be prolonged and made chronic. Thus examples of overtreatment with astringent lotions (copper and zinc sulphate) and alcoholic solutions of aniline dyes and of intolerance to mercurials or sulphonamides are not uncommonly seen.

The bacteriology of impetigo has been investigated for some seventy years, and both beta haemolytic streptococci and *Staphylococcus aureus* and *Staph. albus* are regarded as causal organisms. It seems probable that, at different times and in different countries, one or other organism has been responsible for particular epidemics. *Staph. aureus* is the organism found in impetigo contagiosa neonatorum (pemphigus neonatorum) and in outbreaks in adults. The organism gives rise to small blisters which rupture to form circinate lesions with active blistered edges. The streptococcal types show much more oozing and are covered with thick yellow horny crusts. In the latter type mixed infection is found and it becomes difficult to decide which is the primary organism.

Impetigo, particularly the staphylococcal type, has a great natural tendency to spontaneous cure providing that lesions are kept dry and that, in severe cases, general rest is ensured. There must be no undue trauma of the affected areas of skin, no scratching and picking, and the rough removal of crusts must be avoided. Bases in which drugs are applied to the skin should be designed to allow easy application and removal, and to avoid spreading of infected discharges to neighbouring skin. No form of treatment is likely to succeed in a reasonable time unless it is skilfully and carefully carried out, and the cleansing of crusts and oozing areas performed gently.

Treatment must include attention to cleanliness of clothing and bedding. Brain suggests soaking a handkerchief in perchloride of mercury, 1 in 2,000, pinning it when dry to the pillow, and powdering with talc. The application of simple talcum or zinc oxide powders, of calamine and kaolin lotions and of calamine and zinc drying pastes will give satisfactory results in the majority of cases and treatment becomes, in the main, a nursing problem.

In pre-war practice, the duration of impetigo was found to be eight to fourteen days. The more severe heavily-crusted cases (especially those in which the orifices such as nose and ears were affected, and when the scalp was involved) might be expected to last up to twenty-one days. Some dermatologists would have given a shorter period than this for cure.

With the sulphonamides, the time for cure is seen to vary from three to eight days, and the investigators are agreed that the duration is shorter than would be expected with other methods at their disposal. However, the factors of hospital treatment, rest and cleanliness must be remembered. It is difficult to estimate how much the cure in any particular case is delayed as a result of an acquired resistance.

Sulphanilamide, sulphathiazole and sulphadiazine have all been used in ointment for local application in cases of impetigo in which streptococci have been found, and the response has been favourable. Some have found sulphathiazole and sulphadiazine superior to sulphanilamide, probably because of their inhibitory action on the accompanying staphylococci. It has often been reported that with concentrations of the drug higher than 5 per cent the incidence of local reactions has been greater. According to E. L. Keeney, R. H. Pembroke, F. E. Chatard and J. M. Ziegler (1941), sulphathiazole in 5 per cent concentration was as effective in treatment as were the higher concentrations. The sulphonamide should not be used for longer than six or seven days because local sensitization may develop.

The indication for the use of sulphonamides by mouth would be the persistence of an extensive crusted impetigo, particularly in a patient with a seborrhoeic skin or associated eczema, with rapid increase in the numbers of lesions, or with an inflammatory halo of redness and swelling around the lesions, suggestive of a cellulitic reaction. The latter condition must be carefully distinguished from a dermatitis due to treatment with, say, a mercurial, a sulphonamide or an astringent lotion.

Brain and others have discussed the importance of the vehicle in which the sulphonamide or other drug is to be applied to the skin. The emulsifying bases of the lanette wax SX type (cetyl alcohol) allow of the ready emulsification of oil in water so that creams and pastes incorporating various drugs can be made with saving of lanolin and paraffins. These pastes or creams are readily removed from the skin with soap and water without preliminary softening with vegetable oils or liquid paraffin. Another important feature of these bases is that medicaments incorporated in them are more active than in the normal greasy bases, and that they will absorb serous discharges. G. H. Percival (1943) gives the formulas of three bases which have been used in his clinic.

The newer 'cleansing agents' which are powerful emulsifiers have aroused interest. They are useful for removing crusts, scales, ointments or organisms from the skin, and for the rapid removal of grease, dirt and organisms from vessels used in dressings. Among these cetyltrimethyl-ammonium bromide (C.T.A.B.), may be mentioned. It is bacteriostatic and stated to be as good an antiseptic as most chemicals used on the skin, and it is painless on raw surfaces. Its use has lightened the work in the skin wards, and has helped in the serious problem of cross-infection. Percival has detailed other skin-cleansing compounds.

Treatment of impetigo with strong astringents is suggested from time to time. These include zinc and copper sulphate solution, silver nitrate solution, silver nitrate stick and liquor ferri perchloridi fortis. In general, these astringents can be used only when lesions are few and resistance is good, that is, when equally good results could be obtained from simple cleansing, powdering and drying. Smith (1942) has advocated the use of liquor ferri perchloridi fortis which rapidly penetrates the crust making it firm and hard, but where the oozing areas are extensive it produces too much pain to be of practicable use.

To sum up, the recent literature has clarified the division of impetigo into types with regard to their bacteriology, and has supported the use of sulphonamides in the local treatment of persistent and crusted lesions. In view of the shortage of supplies, substitutes for some of the vehicles used for the application of medicaments are suggested, and some of these present considerable therapeutic advances. They are more easily applied, drugs are more active in them, and they are readily removed with soap and water or with the newer cleansing substances. The action of the latter is rapid and does not demand friction which is often harmful to inflamed and sensitive skin.—L. FORMAN.

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 Steigman, A. J. (1942) *Lancet*, 1, 632.

INDUSTRIAL MEDICINE

Fatigue

Ophthalmic strain

Effect on output.—In his presidential address to the North Transvaal Branch of the South African Medical Association H. de Villiers comments on the probability that more people are thoroughly tired at present than ever before in the history of the world and points out that these people frequently come under the purview of the ophthalmic surgeon. Tiredness and visual difficulties are often related and either may be the cause or the effect of the other. Thus in children astigmatism or other defect may entail so much effort in reading that the child becomes fatigued and will not try to read. In young adults complaining of fatigue, glasses to correct a visual defect may be the remedy required. Presbyopia is sometimes a cause of fatigue and inclination to doze in the evenings in people of middle age. Fatigue in workers due to eyestrain can greatly affect efficiency, reducing their output and increasing their proneness to accidents. The provision of glasses can often resolve their difficulties. Adequate lighting in factories is of great importance. Glare, on the other hand, reduces visual efficiency and is tiring; moreover the eye exposed to glare does not function properly for some time afterwards, and during this period accidents are liable to happen.

Hygiene

Health of the older worker

A. J. Carlson in a paper read before the Annual Congress on Industrial Health, Chicago, emphasizes the following facts about the older industrial worker. Physiological age does not necessarily correspond to chronological age. While most workers over fifty or sixty have somewhat less physical strength and endurance and some impairment of sight and hearing, this may be compensated for by greater skill and experience and reduced tendency to youthful excesses. By keeping in idleness people who are still fit to work, valuable human resources are wasted and the worker himself is allowed to deteriorate into a hanger-on of society, lacking in courage and enterprise. Since owing to senile changes in the neuromuscular system and eyes the older worker tends to become slower, his wages should be scaled down as his capacity diminishes. Otherwise the tendency is either for the more efficient workers to set their pace by that of the less efficient or else for the management to discard the older people. Diet should be adjusted to avoid either emaciation or obesity, both of which shorten life and impair physical performance. Moderation in all things and medical overhaul twice yearly will aid the older worker in keeping fit to carry on.

Prophylactic measures

Efficient lighting

Problems of glare and colour.—The problem of industrial lighting in war-time is considered by C. E. Ferree and G. Rand from two aspects, efficiency and the black-out regulations. The chief object of efficient lighting is to increase production. Highly intense light will, however, quickly fatigue the eye unless it is well diffused and unless glare is eliminated. Fixtures provided with glare baffles or louvres should be fitted and the general illumination supplemented with local lighting where it is necessary. The authors have designed a fixture for local lighting which eliminates glare both from the lamp itself and from the surface of the work. The colour of the light should be as close as possible to that of daylight. The problem of lighting for the black-out is much simplified by the use of lamps similar to those described above. Coloured bulbs may be advisable because with the bulbs now available it is difficult to cut down sufficiently the intensity of white light. The best colour for this purpose has still to be determined and an apparatus for testing lights of different colours is described. With properly shaded lights ordinary curtains can be used and the problem of ventilation under blacked-out conditions becomes less formidable.

Health of women in industry

Recommendations of U.S.A. committee.—The Committee on the Health of Women in Industry appointed by the Section on Obstetrics and Gynecology of the American Medical Association has issued a preliminary report. The following are its chief comments and recommendations. (1) The type of work given to women must not be beyond the physical capacity of the individual. Women, especially mothers, often have to do their housework as well as their factory job and may thus be subjected to excessive burdens. Complete physical examination should be carried out before work is assigned. (2) The clothing of the woman worker should be supervised from the standpoints of safety and comfort. (3) The maximum hours of work should not exceed forty-eight a week. (4) Rest rooms should be provided; rest periods are desirable and may be conducive to increased production. (5) Adequate supervision of women employees is of great importance. (6) Pregnancy demands additional precautions. The pregnant woman must not be overburdened physically or exposed to any substance which might induce abortion or injure the liver or kidneys. She should cease work from the thirty-second week of pregnancy until six weeks after delivery. Lactation is almost always a bar to

employment in industry. (7) Menstruation is a contra-indication to work only if accompanied by severe dysmenorrhoea. In this connexion adequate rest facilities are desirable since a brief interruption in the day's work may prevent loss of several hours. (8) Women at the menopause may need special consideration. (9) The care of children of mothers in industry requires the provision of proper facilities and trained attendants.

The fur industry

Associated diseases

Trauma, dermatosis, asthma; respiratory disease.—The results of a survey of the fur industry undertaken for the New York State Department of Labor are reported by H. Heimann. His conclusions, based on the examination of 694 workers, are as follows (1) Traumatic affections of the hands occur among fleshers, unhairers, hand-stretchers and nailers. They include onycholysis and calluses or denudation of areas exposed to friction. In general they are disfiguring but not disabling, although denudation may cause great discomfort. (2) Dermatitis or a history of dermatosis was found in thirty-five people. It occurs in those who handle dyed skins. All patients reacted positively to patch tests with the appropriate dye. (3) Asthma occurred in thirteen persons, all of whom had worked among dyed skins; it was thought to be occupational in ten. (4) Acute and chronic non-specific respiratory disease of the upper passages appeared to be abnormally frequent. (5) There was not any evidence that the incidence of pulmonary tuberculosis is increased in the fur industry.

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INFANT FEEDING: THE FEEDING OF NORMAL INFANTS AND CHILDREN

See also B.E.M.P., Vol. VII, p. 136; and Cumulative Supplement, Key Nos. 749-753

Principles

Digestibility

Optimum hydrogen-ion concentration.—P. L. Rothman, D. C. Widener and W. C. Davison have tested thirteen specimens collected from two infants (age not stated) in order to determine the optimum hydrogen-ion concentration for the amylase of the duodenal contents in infancy. In a first series of observations the amylase activity was determined viscometrically at a temperature of 34° C., the substrates used being from 2 to 6 per cent suspensions of Lintner soluble starch in twentieth-molar solution of sodium and potassium phosphate at hydrogen-ion concentrations of from 4.9 to 9.0. Below pH 3.0 partial precipitation of the starch suspension was found to occur, but at reactions between 3.0 and 9.0 the viscosity remained almost unaffected. The results of the titrations were plotted and the number of units of amylase per cubic centimetre calculated. The hydrogen-ion range at which the greatest amylase activity occurred was found to be between pH 6.2 and 8.0, with a mean of 6.9. In a second series of experiments eighteen titrations were made upon the duodenal contents of one of the babies at hydrogen-ion concentrations of from 4.8 to 8.6. The results were somewhat irregular, probably because the specimen had been kept in the refrigerator for six weeks, but the mean value appeared to be about 7.0.

Breast feeding

Quantity of milk secreted

Mechanism of lactation.—Mavis Gunther describes some observations on lactation in women. The response of the mammary gland to pregnancy appears to be due to the action of oestrogens, and it can be reproduced by administering oestrogenic substances to virgin animals. Progesterone probably plays a synergic part. After delivery breast secretion gradually increases and changes in character, and true milk secretion is established by about the sixth day. The initiation and maintenance of milk secretion seems to depend upon a hormone, prolactin, which is secreted by the anterior lobe of the pituitary gland. Oestrogens inhibit lactation and the onset of the latter may depend upon the sudden removal of their influence. Secretion is a continuous process but is quickly inhibited if suckling is discontinued. Engorgement of the breast possibly exerts an inhibitory influence. The expulsion of the milk from the breast is a complicated process depending upon the efforts of the baby, especially the milking action of its tongue and lips, and upon a reflex action of the organ itself.

A study of 1,100 cases of failure of lactation has been made by Margaret Robinson. Preliminary observations showed that the normal cycle consists first of a period of filling, lasting from ten to thirty minutes; secondly a period of emptying, lasting usually from five to seven minutes, rarely as long as ten minutes, during which the milk issues in rhythmic jets at the rate of from forty to sixty jets per minute; and thirdly a refractory period of from two and a half to three hours. The pumping mechanism in the emptying phase goes into action spontaneously if feeding is delayed and the breasts become over full, and in one breast when the other is stimulated. Evidence has been adduced that the pumping mechanism is controlled by the posterior lobe of the pituitary gland. The types of failure are

classified as follows. (1) Dry. Milk secretion may completely fail, sometimes quite suddenly, or it may fail to increase in proportion to the infant's needs. In cases of gradual failure the amount of secretion appears to be inversely proportional to the amount of muscular exercise taken. Muscular relaxation, such as that which occurs when a hot bath is taken, seemed to encourage secretion. (2) Wet. During or just before the period of failure secretion is profuse, sometimes continuous, but watery. The breasts are soft and appear to be unable to retain milk. (3) Solid. In a small number of cases the breasts were tense to the touch and on manual expression beads of thick creamy excretion exuded, but pumping did not occur. The breasts appeared to be capable of forming the solid part of the milk but incapable of rendering it liquid. (4) Alactea: complete absence of lactation is rare; it occurred four times in the author's series. Apart from prematurity, which seemed to be related to scanty lactation, and from acute illness or debility of the mother, which together accounted for only 9.9 per cent of the cases, no causal factors came to light. (See also p. 262.)

General management

Avoidance of unnecessary weaning—C. McNeil draws attention to the special importance in war-time of the waste of breast milk caused by unnecessary weaning of babies. The normal process of breast feeding a baby includes lactation, suckling and digestion, and difficulties may arise in connexion with any of these. The great majority of difficulties occur towards the end of the first week; most can be overcome. *Maternal difficulties.* (1) Psychological problems of fear, anxiety and so forth. This group can be greatly reduced by reassurance and persuasion of the mother. (2) General physical illness. The deciding factor is the condition of the mother. Maternal tuberculosis alone is an absolute bar to nursing. (3) Engorgement of the breasts is easily overcome. Mastitis with abscess formation requires temporary suspension of breast feeding. (4) Nipple conditions include fissure, necessitating temporary suspension of suckling; and retraction, which cannot always be overcome. (5) Scanty lactation. This can be verified by test feeding. It is treated by shorter and more frequent sucklings, improving the mother's nutrition and giving supplementary feeds small enough to keep the baby hungry while preventing loss of weight; these measures are not always successful. (6) Mismanagement of nursing may be overcome by instruction and practice. *Infantile difficulties.* (1) Unwillingness to feed; this can be overcome by withholding food (not fluid). (2) Disorders or deformities of the mouth. (3) Vomiting, except in the anaphylactic type the baby should never be weaned prematurely. Vomiting caused by gastric catarrh, due to swallowing of material from the vagina, is treated by giving water only, with a little sodium bicarbonate or magnesia, for twelve hours and, if necessary, by washing out the stomach. Vomiting due to flatulence is entirely a nursing problem. Vomiting caused by excess of milk is disclosed by a few test feeds and remedied by reducing the number and duration of the feeds. Vomiting due to pyloric stenosis particularly calls for continuation of breast feeding, whatever other treatment is adopted. (4) Intestinal flatulence and colic require reduced periods of suckling, slower feeding and care in 'breaking wind'. (5) Frequent greenish stools are a sign of overfeeding. (6) Prematurity may necessitate hand feeding with breast milk. (7) Gastro-enteritis. Feeding is discontinued temporarily and sweetened water is given. Tea is useful. (8) Loss of appetite can be remedied by substituting sweetened water, preceded by a little magnesia, for two or three feeds. (9) Febrile illness occurring in the first month requires cessation of breast feeding for from twelve to twenty-four hours during which period the baby is given abundant sweetened water and tea.

Relation to prenatal diet of mother.—The relation between maternal prenatal diet and ability to breast feed the baby has been investigated by J. H. Ebbs and Helen Kelley. Women attending a clinic were sorted into groups according to the adequacy of their diet. One group of 120 women had a poor diet throughout pregnancy. Another ninety women on an inadequate diet were given extra food from the fourth or fifth month until the baby was six weeks old. A further 170 whose diet was moderately satisfactory were given advice on bringing it up to an approved standard. The ability to nurse was classified as good, fair or poor, the last indicating considerable deficiency of milk or artificial feeding. The percentages of good, fair and poor were as follows. In the poor diet group, 42, 41, 17; in the supplemented group, 52, 42, 6; in the good diet group, 49, 43, 8. The percentage of mothers breast feeding the baby at the end of each of the first six months was highest in the supplemented and lowest in the poor diet group. At six months the average weight of the babies of the second and third groups was slightly above that of the babies of the first group, and they had suffered from fewer illnesses.

Effect of social conditions on breast feeding.—In an attempt to discover whether or not social conditions affect breast feeding, I. Gordon has analysed the information furnished by health visitors in Ilford. His figures relate to three periods, 1920–24, 1930 and 1938. They show a decline in the percentage of breast-fed infants from 87 in both the first two periods to 73 in 1938. The place of breast milk was taken by dried milk. The proportion of infants fed on liquid milk has shown little change but the use of condensed milk has decreased. The duration of breast feeding has diminished even more. In the earlier years it was not unusual to find a child aged eighteen months still being breast fed; it is now rare to find one still breast fed when over nine months old. The poorer districts showed a larger decrease in the number of infants breast fed at six months than did the better-off districts, the difference amounting to 8 per cent. The infant mortality rate has fallen from 54 per 1,000 (1920) to 36.7 (1938). It is a paradoxical fact that as communities become more civilized, breast feeding and infant mortality rates tend to

decline together. The use of infant welfare clinics has greatly increased during the period under consideration. In 1920 for every 100 children born in the borough fifty-three new attendances were registered; in 1938 for every 100 births the new attendances totalled 109, that is children were being brought to the clinics from outside the borough. The percentage of breast-fed babies attending the clinics was less than in the borough as a whole, showing the tendency of the poorer mothers to accept free or cheap milk and to give up what is actually the cheaper and easier course of breast feeding. To determine whether or not the stress of air raids made any difference to breast feeding the records for 1940-1 were examined but the figures did not show any significant difference. Thus, in 1938, the percentage of breast-fed infants at the health visitor's first visit was 73, and at six months 44. In 1940-1 the respective percentages were 71 and 46. From 1920-4 till 1940-1 the percentage of partially breast-fed infants has increased from 3 to 9.5.

Premature weaning.—Margaret Robinson has published the results of an investigation on breast feeding in 1,100 cases of premature weaning, the criterion being cessation of breast feeding before the end of the seventh month. In about 40 per cent of the mothers clinical causes could not be found; some mothers had fed their other children satisfactorily. The following four types of failure are described. (1) Dry, which may be partial or complete, and in which the total secretion is inadequate. A partial deficiency may be due to a deficiency in the mammary gland tissue; complete failure is more common and may be either very sudden (between one feed and the next) or gradual; the controlling mechanism of the whole cycle seems to be at fault. Regular suckling at the empty breast does not prevent failure but rather hastens it by incurring worry. (2) Wet, in which the mothers note that the milk resembles 'blue water', and that the breasts are soft, with persistent and distressing lactorrhoea, which suggests endocrine hyperactivity in the mechanism of emptying. (3) Solid type; the breasts are heavy and nodular and the baby refuses to suckle or to empty the breasts. The secretion is thick and creamy but the normal pumping action responsible for emptying the breast is absent. The defect seems to be both in fluid secretion and in emptying. (4) Complete absence of lactation, or alactaea; this is rare, and in the four cases observed it occurred after a difficult labour. Health conditions in the mother were nearly three times as common a reason for failure as were causes associated with the infant or with environment. Nearly 66 per cent of the mothers suffering from debility were unable to feed the infant after the first month, and this was also true of mothers with flat nipples or mastitis. A definite relation existed between muscular activity and reduction of milk secretion; prematurity seemed to favour scanty secretion but another pregnancy and menstruation did not appear to have much effect. Further investigations are being conducted as to the effects of prematurity on lactation. (See also p 260)

Working mothers and breast feeding.—A report for the British Paediatric Association has been issued by the Committee (A. V. Neale, Ethel Cassie, Frances Braid and Mila Pierce) formed in Birmingham in 1942 to investigate breast feeding in the city, especially in its relation to female labour. Reports were made by 100 health visitors on the babies born during the first quarters of 1941 and 1942. Records were obtained in this way of 4,635 babies, and the results are compared with those obtained in the course of a similar inquiry held in 1938 regarding the babies, 4,378 in number, born in the months January to June 1937. The proportion of babies wholly or partly breast fed for from three to six months was 51 per cent of the 1937 group as compared with 53 per cent of the 1941 and 1942 group. The blame for the low incidence of breast feeding cannot, therefore, be placed upon the war. In the earlier weeks a first baby is at a disadvantage as compared with a second or later child, but after two months the inequality disappears. It is suggested that the difference may be due to the lessened degree of anxiety associated with a second or succeeding pregnancy. Working during pregnancy seems to have little influence on subsequent breast feeding. If the mothers are divided into two groups, those who breast fed the baby for three months or less and those who breast fed the baby for more than three months, the percentage of those who worked during pregnancy is found to be 17.7 in the first group and 14.3 in the second. The number of women who return to work after confinement is small, amounting to only 12 per cent of the total. Corroborative evidence is found in the small number of young infants admitted to day nurseries. Most of these came from districts where the women were accustomed to go out to work before the war and, incidentally, where infant mortality rates were high. The percentage of infants breast fed for less than a month, or not at all, fell from 13 in the 1938 group to 7.5 in the 1941 and 1942 group. Illegitimate children are believed to account for a large proportion of these cases. When the babies were divided into 'sick' and 'well', according to the state of their general health, it appeared that of the former group 48 per cent were weaned by the end of the first month and 80 per cent by the end of the second month, while the respective percentages for the latter group were 34 and 35. Present influences which are adverse to breast feeding were decided to be as follows. (1) The doctor, who was found to be more than any other single factor responsible for weaning babies; doctors are apt to take babies off the breast whenever any difficulty arises, instead of trying to solve the problem of successful breast feeding. Doctors who made a practice of this were named. (2) Queuing for shopping. (3) Emotional disturbances, especially anxiety about husbands. (4) Part-time work; a further inquiry regarding 164 babies attending the Children's Hospital during September 1942 showed that early weaning is associated with gastro-enteritis and with early infections.

Control of milk outflow

The draught reflex.—H. K. Waller presents evidence for the existence in women of a reflex controlling the outflow of milk from the breast. (1) Of fifty-two women questioned, forty-six said that milk was plentiful in the first puerperal week, but that withdrawal was difficult and incomplete. (2) Samples of milk were taken at the beginning and at the end of nursing from both breasts of twenty-six women. In cows a sudden rise of tension within the udder, probably due to reflex venous engorgement, occurs at the start of milking. This forces the fat-laden milk in the alveoli out into the ducts. If the four quarters of the udder are milked in turn a considerable difference is found between the fat content of the 'fore' and 'hind' milk in the first quarter milked, but the difference, owing to diffusion, is almost obliterated when the fourth quarter is reached. The human samples showed an average rise of fat in the 'hind' milk from the first breast of 4.2 per cent, and in the 'hind' milk from the second breast of 1.9 per cent. This reflex is known as the draught reflex. It is subject to interference and conditioning, and especially may be suppressed by overloading of the breasts.

Feeding reflexes

Analysis of instinctive behaviour.—C. A. Aldrich finds the new-born baby 'squirming on the horns of a dilemma': primitive instinct versus authoritative routine. The normal child at birth is equipped with various reflexes or behaviour patterns. One of the first to come into play is the rooting reflex: if one cheek is touched by a smooth object the baby turns his mouth in that direction and opens it in expectation of grasping the nipple. This gives a clue to the right method of offering the breast. The sucking reflex, which comes into action when the baby grasps the nipple, develops *pari passu* with the swallowing reflex. The latter involves the highly complicated process of transporting the milk past the opening of the larynx. The importance of the swallowing reflex is most apparent in premature or weakly babies, in many of whom the food is liable to go down the windpipe. The satiety reflex causes the baby to stop suckling when he has had enough. He should not be restricted in the quantity of his feed, nor forced to take more than he wants. Night feeds should be continued until he voluntarily gives them up. Closely allied to the satiety reflex is the hunger mechanism. A baby should be allowed to eat when he cries with hunger pangs, not made to wait for some arbitrarily fixed moment at which, crying or sleeping, he is picked up and fed. At three to four months the fact that he can now take thick foods is shown by his learning to open the mouth to a spoon. At about six months chewing movements begin, and mark the time when solid foods can be given. Meanwhile the child begins to use his hands with greater skill and by about eighteen months should be able to feed himself with a spoon. After this, the more he is left to himself at meals the better.

EDITORIAL COMMENTARY—Infant Feeding Problems of Today

The importance of breast feeding has been emphasized in a recent Report (vide supra) on the subject prepared for the British Paediatric Association by Neale, Ithel Cassie, Frances Brand and Mila Pierce. They conclude that war-time conditions have not materially altered the incidence of breast feeding in Birmingham. Their inquiries showed that very few women were prepared to leave their homes and go to work (unless economic circumstances made it imperative) while the baby was under the age of six months, and that only 50 per cent of women were prepared to continue breast feeding their baby after it was three months of age.

H. K. Waller's *Clinical Studies in Lactation* and his communication in the *Lancet*, 1943, deserve the attention of all those responsible for the care of infants and the management of breast feeding. The reason why lactation fails in a high proportion of women has never been clearly understood; in the Birmingham report referred to above, the health of the mothers and faulty advice from doctors was blamed. Waller concentrates on the causes of failure in the first four weeks. He shows that the first milk from the breasts is thin and the late milk contains much fat. He emphasizes what is not sufficiently realized—the force with which the milk flows or is ejected from the nipple at the time of feeding, even before the infant is put to the breast. The mother may feel the draught or a tightness or tingling in the breast, followed by the expulsion of the milk. This is a conditioned reflex and probably what happens is that the smooth muscle which is present in the human breast, particularly around the large lactiferous ducts and also around the alveoli contracts, causing increased pressure in the breasts. Gunther suggests that the draught is accompanied by peristaltic waves passing down the ducts towards the nipple. Probably in the past too much emphasis has been placed on the sucking of the infant and insufficient emphasis on the expulsive power of the breast itself.

It appears that even before labour has commenced the lactiferous ducts should be emptied of their dry serum and milk and in this way they are widely patent. Once lactation is established the breasts must never be allowed to become engorged, lest from back pressure the power of the acini to secrete milk be destroyed. Mavis Gunther (1942) comes to the same conclusions after researches in Canada. It is when the breast is over-filled and the infant unable to suck at it properly that damage is done to the nipple, and breast abscesses result. If the ducts have been emptied thoroughly in the last few weeks of pregnancy, and someone is on the look-out to prevent engorgement of the breasts by expressing the milk by hand, back pressure is prevented and lactation is a success. The situation will not improve until the obstetrician, the maternity nurse and the midwife also fully realize their responsibility in this direction. Waller feels that the management of lactation may need to be adapted far more

closely to the individual woman than is the custom at present. In order to prevent engorgement it may be necessary, for instance, to put the infant to the breast in the first few days at shorter intervals than is the rule at present.

War conditions have brought about the admission to hospital of many cases of feeding difficulties which probably in peace-time would not have been admitted. For various reasons the mothers of the infants have been admitted with the baby. Experience has shown that to offer detailed advice to the majority of these mothers is a waste of time, as in hospital it is discovered that they lack confidence and knowledge of even the simplest fundamentals and require practical instruction. The majority of the problems have been in the bottle-fed cases and it has required perhaps a week's tuition in hospital, under the skilled guidance of a clever nurse, to teach the mother sufficient of the technique of bottle feeding and to restore her confidence in her ability to do this. On the other hand, the weaning of an infant underfed on the breast has often been prevented by instructing the mother in test feeding and the giving of complementary feeds. In such instances, it is necessary to supply the mother with scales in her own home; unfortunately for the time being there is a lamentably inadequate supply of such scales. Instruction by a competent health visitor in the patient's own home would be successful in a proportion of the cases. Feeding difficulties in the first few weeks of life must be taken much more seriously by the medical profession and not left entirely in the hands of the maternity nurse and health visitor.

It is suggested that the ideal should be for each woman to leave the maternity hospital (1) breast feeding her baby, (2) able to manage the infant, and (3) happy; in fact, anxious to return to have her next baby. This could be brought about only by a further week's stay in hospital where, with her baby to herself, and in her own cubicle, she could learn to bath it, change it and feed it, and therefore she would go home full of confidence in her ability to do these things properly. At present many women are spending a week in a children's hospital, learning to bottle feed their babies, whereas they might far better have had a further week in the maternity hospital learning to breast feed it.—DONALD PATTERSON

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INFLUENZA

See also B.E.M.P., Vol. VII, p. 173, and Cumulative Supplement, Key No. 754.

Ætiology

Filter-passing virus

Comparison of influenza with other virus diseases—At a meeting of the Fever Hospital Medical Service Group of the Society of Medical Officers of Health S. P. Bedson opened a discussion on recent work on the virus disease. The demonstration by Smith, Andrewes and Laidlaw ten years ago that epidemic influenza was due to a virus (now known as the influenza A virus) stimulated the hope that a specific prophylaxis might be made available to control this disease. That this has not been fulfilled is due to two main facts: the virus of Smith, Andrewes and Laidlaw (now known as influenza A virus) was not the sole cause of influenza. Influenza virus has been found to comprise a number of serological types, and a second virus, influenza B virus, has been identified. Influenza A virus is still the most important ætiological agent. An efficient multivalent vaccine is difficult to prepare, and a combination of influenza A virus with a particular strain of distemper provided a promising broad antigenicity covering all the serological types; but this bivalent vaccine had given but mediocre results. Primary atypical pneumonia had given rise to several outbreaks especially since the beginning of the present war. A virus known to cause primary atypical pneumonia in man, has been the virus of psittacosis which is now recognized not to be confined to the parrot family of birds; it may occur in pigeons and in the fulmar petrel and has been discovered to spread from cats to man. A large group of viruses belong to the psittacosis family and it has therefore been suggested that the name ornithosis should be substituted for that of psittacosis. Some cases of primary atypical pneumonia are due to virus infection. Lymphogranuloma venereum belongs to the psittacosis group of virus infections. Speaking later in the discussion C. H. Andrewes said that if the best possible influenza A vaccine be injected shortly before an influenza epidemic it might be hoped that a 50 per cent fall in the incidence of influenza would result.

Clinical picture

Comparison of the three epidemiological types

Ineffectiveness of drugs and vaccines.—F. L. Horsfall, Jun. enumerates the chief unsolved

problems in connexion with influenza as follows: incomplete information concerning its cause; inadequate criteria for differentiation of the several varieties; lack of effective means of prophylaxis and treatment. Influenza appears in three epidemiologically distinct forms, pandemic, epidemic and endemic. Pandemic influenza seems to have recurred at irregular intervals for many centuries. The cause is unknown. Bacterial infection of the respiratory tract increases the mortality. The sulphonamide drugs may prove to be of value in future outbreaks in combating this type of secondary infection. Epidemic influenza seems to be much milder than the pandemic form. During the past decade outbreaks have tended to occur in the winters of odd-numbered years. Three varieties are distinguished, caused respectively by virus A, virus B and by an unknown agent or agents. The third type is known as influenza Y. Both virus A and virus B are infectious for several species of animals as well as for man. For influenza A the incubation period is twenty-four to forty-eight hours. The virus can be obtained from the nasopharynx during the first week of the disease. It has not been demonstrated in the blood stream. Secondary bacterial infection is very rare. During convalescence a pronounced antibody reaction against virus A occurs, which reaches its peak about two weeks after the onset of the illness. Virus B causes an illness distinguishable from influenza A only on immunological grounds and followed by a similar antibody reaction against virus B. Infection by virus A does not immunize against virus B and vice versa. In a very few cases immunity develops against both viruses. In any given epidemic cases of all types occur. Endemic influenza affects large numbers of people each winter. Clinically indistinguishable from epidemic influenza, it appears to be due to neither A nor B virus. Secondary bacterial infection, especially of the paranasal sinuses and bronchi, is common. Immunity following an attack of any type is short lived. Repeated attacks have occurred at intervals of no more than two years. Vaccination confers very transient immunity; with influenza A it appears to last for about a month. There is no known drug which influences the course of the disease.

Treatment

Preventive

Review of prophylactic methods.—T. Francis, Jun., in a Clarence M. Jackson lecture, deals with the control of epidemic influenza. The reservoir of this disease has not been detected, so that the only resource at present is to deal with outbreaks as they arise. Influenza spreads by transference of the virus from person to person, usually by direct infection. The infection is primarily superficial, attacking the epithelium of the upper respiratory passages. Pneumonia appears to be a secondary phenomenon. Attempts at active immunization have on the whole given disappointing results. Vaccination by the intranasal route holds out greater hopes of success and deserves further trial. Passive immunization by the intranasal application of immune serum may be valuable during epidemics. Other methods include sterilization of air by means of ultra-violet light or aerosols, the latter being of greater practical applicability. Masks of proper design, worn by influenza patients or by susceptible contacts, are of great value in prophylaxis.

The fugitive influenza viruses.—A Leading Article in the *British Medical Journal* discusses recent work on immunization against influenza. The problem has become more complicated as more facts have emerged. It is now known that clinical influenza may be caused by at least two unrelated viruses and by agents as yet unidentified. The two viruses are termed A and B, and influenza from which neither can be isolated is known as influenza Y. The first two are immunologically distinct, a high blood content of antibody to the one leaving susceptibility to the other quite unaffected. Evidence has been obtained, moreover, that the higher the degree of immunity to either of the known viruses the greater the susceptibility to type Y. Passive immunization experiments have yielded conflicting results: in some cases the incidence appears to have been reduced, in others unaffected. Immunity however produced seems to be extremely fugitive. After vaccination the antibody titre of the blood quickly declines and on the other hand repeated attacks of influenza A have been observed within a short time. Certain experiments suggest that living virus is a more effective immunizing agent than inactivated virus. In general, however, immunization against influenza has little claim at present to be regarded as a satisfactory procedure.

Experiments with various remedies.—Measures for the control of influenza have been the subject of experiments by J. Stokes, Jun. and W. Henle. Infection being in all probability airborne, disinfection of air was first tried. The room used was a large empty ward divided by partitions reaching to within four feet of the ceiling into sixteen cubicles, open in front. Two methods of disinfection were used, ultra-violet irradiation and propylene glycol vapour. The arrangements for irradiation provided a curtain of ultra-violet rays in front of each cubicle and a ceiling of rays above the tops of the cubicles. Propylene glycol was vaporized from an electric hot-plate placed in front of an electric fan, the concentration being from 1 in 2,000,000 to 1 in 4,000,000. During the experimental periods, each lasting 150 minutes, the doors and windows were kept closed and a highly mouse-virulent suspension of influenza A virus was sprayed into the air. Cages each containing ten mice were placed close to the back wall of seven of the cubicles. During the first experimental period ultra-violet light was tested, during the second no disinfecting agent was used, during the third propylene glycol was vaporized. Between the second and third periods, and in order to sterilize the air, the ultra-violet light was first turned on and propylene glycol was then vaporized for thirty

minutes. The results were as follows: the entire control group of seventy mice (the second lot exposed) succumbed within ten days, all having typical influenza lesions. With ultra-violet light, only three of the seventy mice died; these had all been in the same cubicle as the atomizer and the remaining seven mice from this cage when killed on the tenth day showed varying degrees of pulmonary consolidation. Twelve additional mice which had been in adjacent cubicles showed slight pulmonary involvement. The forty-eight remaining mice had no influenzal lesions. With propylene glycol all the mice survived and only three, all from the cubicle containing the atomizer, showed influenzal lesions when killed on the tenth day. Three mice died from other causes. Prophylactic vaccination with inactivated A virus was tested in a group of seventy-two schoolboys occupying a single house. Forty-four were vaccinated, twenty-eight acting as controls. About a month after the last had been vaccinated all were made to inhale for four minutes, through aviation oxygen masks, an atomized suspension of A virus. Among the boys of the control group, clinical influenza developed in ten (35 per cent). In the vaccinated group only one case of clinical influenza occurred, and it had been noted in the boy concerned that the antibody titre of the blood prior to exposure was very low. Subclinical infection, as evidenced by temperatures of 99° F. or over, occurred during the first few days after exposure in a large proportion of both groups. A considerable number showed a leucopenia. No other signs or symptoms were noted. Passive immunization with serum from convalescent or vaccinated individuals was found to afford a considerable degree of protection in mice, especially when given by inhalation. Experiments in the production of concentrated immune sera are proceeding.

Planning for defence against influenza.—In a Leading Article in the *Lancet* the suggestion is made that plans should be made now to deal with a possible future pandemic of influenza, and the means available are discussed. The value of quarantine regulations is very doubtful even if from a practical point of view they were feasible. Vaccination with virus A has given conflicting results and appears to be more effective against experimentally produced infection than against the naturally acquired disease. It seems unnecessary, therefore, to build up large stocks of virus A vaccine, especially as the exact nature of the virus responsible for pandemic influenza is as yet unknown. Australian workers suggest that an attenuated strain of virus might be produced which, given intranasally in the living state so as to produce subclinical disease, might lead to immunity against the serious type of influenza. It has been shown that such an attenuated form of virus B given intranasally produces few or no symptoms of influenza but causes the antibody titre to rise. Passive immunization of the respiratory tract by spraying with immune serum has been tried in Moscow on human volunteers, an apparatus being used from which fifteen people at a time could inhale the atomized serum. Striking reduction in the incidence of influenza is claimed. Antiseptic sprays and ultra-violet light have given encouraging results; propylene glycol vapour appears to be particularly effective in reducing air-borne infection. Experimentally in animals exposed to atomized influenza vapour and clinically in children these methods of disinfecting the air were found to be equally successful. The conclusion drawn from this survey of the means at hand for controlling pandemic influenza is that disinfection of air is the most hopeful possibility in the present state of knowledge. Intensive study of the next pandemic when it comes may place better weapons in our hands for preventing the next but one.

EDITORIAL COMMENTARY—The Influenza Problem

The vast literature which has accumulated around so-called influenza presents unusual difficulties to a reviewer, as exact knowledge is all too slender, being often obscured by conflicting views and data and uncertainty concerning the actual disease referred to. The designation, influenza, is used not only for *epidemic influenza*, which is of virus origin, but also for *febrile catarrhs* and various other ailments. While differentiation between these conditions would obviously be of clinical and epidemiological value, it is unfortunately not always practicable. The main points in differential diagnosis are that cases of virus infection tend to have a sudden onset without preceding catarrhal symptoms, while constitutional symptoms such as headache, malaise and muscular pains are usually prominent; in the febrile catarrh type of infection the onset is more gradual, coryza, cough and sore throat tend to predominate, and constitutional symptoms are less evident. Epidemic influenza is due to various strains of virus, namely *virus A* isolated in Great Britain in 1933, *virus B* isolated independently in the United States of America in 1940, each having its several substrains, or other viruses not yet identified but classified together as *influenza Y*. It is probable that the pandemic of 1918 was of virus origin. The passage of a virus of low virulence through very susceptible persons may lead to enhancement of virulence and epidemic spread: *febrile catarrh* amongst the population may have a predisposing influence.

As influenza is spread by droplets from patients and probably also from healthy carriers, the isolation of infected persons is an obvious method of control, but has distinct limitations. Masks of special type, with an impervious layer (paper or cellulose acetate) between two layers of linen made in the form of a pouch, are of value for nurses and other attendants, but are too uncomfortable to be worn by the community generally. The prophylactic value of gargling, combined with nasal douches or sprays, is unproven, and the use of aerosol mists is a poor substitute for good ventilation.

The problem of immunization against influenza is complex, as a number of viruses and even

of substrains are concerned; present methods of vaccination have only a limited value. Living mouse virus and tissue culture virus, injected subcutaneously or intraperitoneally, confer temporary protection on ferrets and mice against the homologous strain, but are of doubtful benefit to man, although they increase circulating antibody. Intranasal inoculation of living virus produces demonstrable immunity in ferrets, but although the method has been used in man—sometimes causing in the process several typical cases of influenza—it has not yet been tested in a population which has subsequently passed through an epidemic. Virus inactivated by heat or weak formaldehyde is a weaker antigen than living virus, but immunizes ferrets and mice. A vaccine of this type, consisting of formalinized filtrates of infected mouse lungs, or prepared from infected chick embryos, causes only trifling reactions in man and is free from the obvious disadvantage inherent in all living vaccines. Field tests made under suitable conditions with inactivated vaccine are so far discouraging, and the earlier reports that complex influenza distemper vaccine is superior to simple influenza vaccine have not been substantiated.

A single injection into human beings of formalized vaccine usually causes a rise in circulating antibody which is not increased by one or two additional doses at fortnightly intervals. It is puzzling that a high titre of antibody may diminish to only a slight extent an individual's susceptibility to the corresponding virus. Susceptibility to the other known virus is unaffected. An unexpected and somewhat disturbing feature is that the higher the titre to virus A or B, the greater the susceptibility to the unknown viruses (influenza Y). Thus the virus vaccines so far available cannot be regarded as satisfactory immunizing agents. At the best, they protect only against the homologous strain, and evidence points to a multiplicity of strains being responsible for different outbreaks. Again, protection is of short duration and would probably require to be renewed at the beginning of each winter. As outbreaks of influenza do not occur every year, the methods suggested are hardly practicable for mass immunization. Repeated attacks of virus A infection have been observed, indicating that the disease itself does not confer a solid immunity; it is not surprising, therefore, that artificial immunization has been so disappointing.

In considering the influenza problem, we should not overlook the common cold for which other viruses may be primarily responsible. Is it essential to include these viruses in some composite vaccine in any plan of campaign? The secondary symptoms of what is termed influenza or a cold are usually attributed to organisms such as Pfeiffer's bacillus, the pneumococcus or the streptococcus, and coryza vaccines have been prepared from these and other bacteria. The results have been discouraging in field trials in man when regard has been paid to statistical principles, although many clinicians are satisfied with the results obtained in certain individuals. Treatment with the sulphonamides should be useful in most bacterial secondary infections.

The serum therapy of influenza is still under investigation; the results to date have not been promising. It has been claimed that inhalation of atomized antiserum is of value both in clinical cases of influenza and in prophylaxis, but the evidence is not very convincing.—H. J. PARISH.

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INJURIES

Wounds

Surgery

Abdominal surgery.—J. Walton, lecturing on abdominal surgery in war at the British Post-graduate Medical School, deprecates above all uncertainty and indecision; the essentials in operating are carrying out an orderly examination, keeping in mind the frequency of multiple lesions, making a firm decision and taking quick action. For lacerated wounds with protrusion of the intestine, treatment at the first-aid post depends upon the period likely to elapse before the patient reaches a hospital. If it is likely to be long, the intestines should be washed and replaced, the wound dusted with sulphanilamide and closed with a few stitches; if short, a dressing should be applied and the patient sent on. Deliberate treatment consists in cleansing of the wound, with excision of all dead and doubtful tissue. The intestine is then carefully examined; if uninjured it is washed with saline and replaced. If possible, the peritoneum is closed. If the muscle has been much injured the wound is left open, dusted with sulphanilamide and packed. Wounds of the stomach are usually easily closed. Perforations of the small intestine are sutured whenever it is possible to leave viable gut with an unnnarrowed lumen. When the bowel is severely lacerated or its blood supply is severed, or sometimes when multiple wounds are present in a small length of gut, resection must be carried out through normal tissue and anastomosis performed, preferably in end to end fashion. In the colon, wounds are often best treated by exteriorization (temporary colostomy). Wounds of the

rectum and lower part of the pelvic colon should be sutured if possible, and iliac colostomy performed above the injury. Wounds of the bladder may be sutured, but insertion of a tube is often safer. Intraperitoneal bleeding may be due either to crushing or to penetration of a solid viscus. In crush injuries operation is best delayed, unless the patient's condition is getting worse, until shock has been controlled. Wounds of the liver can be sutured with thick (no. 6) catgut. A mattress suture is passed from side to side of the wound and, before it is tied, a piece of catgut is laid under the loops, across the tear; after the mattress suture is tied the second suture is also tied and this serves to draw the two loops together. A wounded spleen is too friable for suture and should be removed. The kidney can be sutured if not too severely lacerated. Abdomino-thoracic wounds can sometimes be dealt with through a single incision, but in some cases the making of separate thoracic and abdominal incisions is necessary in order to deal with all the injuries.

After-treatment of head injuries -- A plan for the post-war treatment of head injuries is outlined by H. Cairns. His chief points are as follows: (1) Plans should be based on a survey of unselected cases. Permanently incapacitating brain damage from head injuries in civilians appears to be rare. An impression is gaining ground in the special centres established since war began that the picture has been painted blacker than it ought to have been. (2) Head injuries should be treated primarily by a trained accident surgeon at a general hospital, the aid of a neurosurgeon being sought if the damage to brain or skull is severe or if recovery fails to take place as expected. It is reasonably certain that the number of head injuries occurring each year is too great to allow of all patients being treated by neurosurgeons. Operation is often required to close scalp wounds, rarely otherwise. Rehabilitation is of great importance. Institutional treatment should not be required for most patients. The patient's personality and social circumstances must be thoroughly studied, and the best person to do this is the surgeon who treated the patient in the acute stages. Specialist psychological treatment is seldom necessary. An important part of the treatment is reassurance of the patient and his relatives.

Incised and punctured wounds -- C. P. G. Wakeley deals with the treatment of minor incised and punctured wounds. In cases of incised wounds seven essentials must be attended to: (1) Arrest of bleeding. General oozing may be stopped by firm pressure. Divided arteries and veins will require ligature except in scalp wounds, in which the interrupted stitches will fulfil the dual purpose of ligatures and coaptation sutures. (2) Sterilization of the wound and its surroundings. In casualty work asepsis is impossible and it is necessary to fall back on antiseptics. The wound and its surroundings must be purified, and for this purpose Dettol is recommended. (3) Closure of the wound by stitching. Silkworm gut or thread should be used. Interrupted sutures are best for small wounds and for scalp wounds. Large wounds are more quickly closed by a continuous stitch of either the glover's or the blanket type. If the latter is used care must be taken to avoid pulling it too tight. (4) Drainage must be provided if necessary to prevent accumulation of blood clot. Badly lacerated or crushed wounds require drainage most often. For small wounds a strand of horsehair or a strip of rubber glove or protective will suffice; for larger wounds a rubber tube should be used. The drain can be removed after from twenty-four to forty-eight hours. (5) All flesh sources of irritation and infection must be excluded by some form of dressing. Attempts to dispense with dressings as a war-time economy have in some cases been followed by disaster. (6) Rest to the injured part must be secured. (7) The patient's general health requires attention. A good purge is often advisable. Vitamin preparations may be given. Stitches are removed on the eighth day, except from the face (four days) or scalp (ten to fourteen days).

Cases of punctured wounds and retained foreign bodies should be dealt with in hospital. As a first-aid measure the wound should be covered merely with a dry dressing. In all cases of wounds in which contamination by soil or road dust may have occurred a prophylactic injection of antitetanus serum, 3,000 units intramuscularly, must be given. The use of sulphonamides must not supplant general surgical principles in the treatment of wounds although, applied locally, the drugs are of value in dirty lacerated wounds when complete excision of all damaged tissue is impossible. They must not be used in conjunction with any antiseptic. It is rarely necessary to use sulphonamides by mouth in the treatment of minor wounds unless sepsis intervenes.

Infection

Local treatment by sulphonamides -- D. N. Matthews reports some experimental studies designed to show the effects of sulphonamides applied locally to human wounds. The twenty patients with wounds investigated were all treated by sulphonamide powder in the form either of sulphanilamide or of sulphathiazole. The number of living organisms present in the wound (the 'viable count') was estimated daily by taking a known quantity of exudate from a carefully noted and easily identifiable place in the wound into an erythrocyte pipette and by mixing it with broth to various dilutions. These were plated out and incubated for twenty-four hours, and the number of colonies present were then counted by holding the plate before a bright screen. The plate chosen for counting was one with a reasonably small number of colonies and, by multiplying the figure obtained by the degree of dilution of the material used to make the culture, the number of colonies which would have grown from undiluted exudate was arrived at. To ensure that growth should not be inhibited by sulphonamide drawn up with the exudate, a small quantity of para-aminobenzoic acid, which neutralizes the action of the

drug, was added to the culture medium. In all cases the viable count was lowered by sulphonamide treatment to a degree varying with the organism involved. The chief drop occurred in the streptococcus count. After a few days the count becomes stationary and may even rise slightly, possibly because the organisms have acquired a degree of immunity to sulphonamides; but the survivors appear to be the less virulent types of organisms and clinical improvement continues. For chronic wounds with indolent sloughs, sulphathiazole appeared to be more effective than sulphanilamide, but the series was too small to allow of dogmatic conclusions. Sulphathiazole gave good results also when applied to tuberculous sinuses. In a further series of experiments the concentration of sulphonamide in the blood was estimated at intervals during the thirty-six hours after the application of a measured quantity of the drug to a wound of known extent. Extremely low values were recorded, lower for sulphathiazole than for sulphanilamide; the effect of the drug appears to be due therefore to local action alone, not to absorption into the blood stream. The concentration in the urine was estimated over the same period, and was found to be considerable, showing that excretion takes place mainly through the kidneys; frequent examinations of the urine for evidence of renal damage is therefore advisable. General toxæmia did not occur in any of the cases. Bivalved plaster cases to ensure rest are an aid to successful local chemotherapy. It must be remembered that various drugs, for example eusol, are antagonistic to the sulphonamides.

Technique of propamidine treatment.—An account of their experiences with propamidine for infected wounds and burns is given by F. Kohn, M. H. Hall and Clara D. Cross. The number of cases (thirteen) is too small for general conclusions to be drawn, but in the authors' view the results have been sufficiently encouraging to warrant further trials. The following technique was used. The wound was first cleaned with saline and examined bacteriologically. The surrounding skin was dried and the propamidine applied evenly to the whole surface of the wound. In most cases the drug was made up in a jelly base, but for some of the burns a Mumford base was employed. The wound was then covered with sterile fine-mesh Vaseline gauze and a thin layer of cotton-wool, and bandaged. The dressing was changed every forty-eight hours. No patient required more than five applications of propamidine to render the wound clean and healthy-looking. A number of the patients had been treated previously by other methods with very little success, and in others it was thought that healing was likely to be very slow under orthodox treatment. Propamidine appeared to be of considerable value in accelerating repair, and especially in hastening the time at which skin grafting could be undertaken.

Treatment methods in various conditions. In the fifty-fifth Thomas Dent Mutter lecture given at the College of Physicians of Philadelphia, H. W. Orr returns to his programme, published in 1923, and mentions that as the popularity of the Carrel-Dakin method declined, there came the turn of mercurochrome, maggots, bacteriophage and now the sulphonamides—all involving disturbance of the wound and damage to the patient. He adds that in the meantime we have begun to talk about healing hormones, supposed to be produced somewhere in the body as a response to muscle or other tissue injury. These, if they exist, are agents which no one has seen, the chemical formula of which is not known, and their *modus operandi* can only be guessed at from results presumably attributable to them or to other substances—names, compositions and whereabouts unknown. It is possible to find a good deal about the conditions under which a patient's resistance to infection and his healing processes operate to the best advantage; this is in the more or less neglected field called by Flexner 'the science of the bedside' or clinical surgery. Just recently a considerable number of wound infections were treated successfully on the lines Orr has advocated; this was done at Pearl Harbour, partly intentionally and partly because of the pressure of circumstances. The wounds were treated with a minimum of primary surgery. During the six months before 2nd June, 1941 Orr had employed acetanilide as a most successful antiseptic. Among other dicta the author points out that to suggest that sulphonamides, so popular now, are more specific, more efficient or more trustworthy than their thousands of predecessors or to give them credit for the benefits due to the open wound or infrequent dressing, is to misunderstand the part played by the patient himself and his defence against infection. The results claimed for wound antiseptics can be obtained regularly without them if the surgical fundamentals of drainage, prevention of infection, rest in the correct position and general care of the patient are always adhered to.

Healing

Importance of sulphathiazole.—Fourteen cases of grossly infected wounds, many of which had failed to respond to other treatments including sulphonamides by mouth, have been treated by H. N. Green and T. Parkin by intensive local application of sulphathiazole powder. In all cases the clinical condition rapidly improved although in most the causal organism was not eliminated. In a further small series of cases the influence of heat upon the bacteriostatic activity of sulphanilamide was investigated. Five septic wounds of the hands were treated by immersion in a saturated solution (about 1 in 90) of sulphanilamide maintained at a temperature of 110–120° F. The period of immersion was one to two hours, and the baths were repeated at intervals sufficiently long to prevent the skin from becoming waterlogged; the maximum daily total period was six hours. In other cases a continuous drip was maintained. The results were very encouraging. Sulphathiazole is the sulphonamide of choice in cases of infection by staphylococci or any other organism not highly sensitive to sulphanilamide. The

advantages of local as against systemic chemotherapy are that a much higher local concentration of the drug can be attained while the blood concentration remains so low that the risk of poisoning is reduced to a minimum. Even with continuous application to large wounds the blood concentration was below 1 milligram per 100 cubic centimetres in most of the fourteen cases, and the highest figure did not much exceed 2 milligrams. The disadvantages of local chemotherapy are as follows. (1) Exudates have an antsulphonamide action, therefore when discharge is copious repeated cleansing and reapplication of sulphonamide are necessary. (2) Sulphonamides are absorbed more or less rapidly from the wound. This again necessitates frequent reapplication. (3) Local damage is a theoretical danger. (4) Penetration of the walls of the wound by the drug may be incomplete, so that it fails to reach organisms imbedded in the tissues. This again is a theoretical objection.

Influence of newer drugs—An Annotation in the *British Medical Journal* draws attention to the present day revival of belief in antiseptics for the treatment of wounds. This revival was set on foot by the success of local sulphonamide treatment, and by the discovery of gramicidin and the rediscovery of penicillin. A distinction must be made between the prevention of infection in a wound in which tissue invasion has not begun and, a matter of much greater difficulty, the termination of an established wound infection. The flavines and related compounds have been shown experimentally to be capable of preventing infection in a wound. Their bactericidal action, although slow, is powerful and they are comparatively harmless to tissues. Proflavine appears to be the most effective of the flavine compounds and in isotonic buffered solution can be applied even to the brain without causing significant tissue damage. It has been found to equal the sulphonamides in efficacy as a preventive of anaerobic infection of wounds. Evidence has recently been adduced that proflavine in solid form is capable not only of preventing but also of curing wound infections. In eighty casualties from Libya, intractably suppurating wounds have been treated with local applications of 0.5 to 2 grammes of proflavine powder, and rapid healing followed in all but six, in one case healing was thought to have been retarded by the treatment. Proflavine acts upon all bacteria found in suppurating wounds, although *B. proteus* is somewhat resistant to it. It is of particular value in staphylococcal infections because these tend to resist other treatment. Many of the cases cited above had received without benefit full courses of sulphanilamide or sulphathiazole by mouth as well as by local chemotherapy. Proflavine powder has also been used in small quantities (0.25 gramme or 4 grains) as a mixture with sulphanilamide powder (2 to 5 grammes or 30 to 75 grains) for prophylaxis of wound infections, but results have not been given. In a recent investigation into the capacity of various antiseptics to inhibit the development of *Clostridium welchii* in mice proflavine was found to occupy a place above sulphanilamide and inferior only to that of penicillin. The successes of proflavine powder are probably related to its comparatively low solubility, about 1 in 300, which is almost ideal for persistence of effect combined with adequate concentration. In the application of any antiseptic solution, whether it is used to irrigate the wound or to soak dressings which are then packed in, cannot secure the penetration and persistence attainable with a slowly dissolving solid.

Local sulphanilamide treatment.—A. R. Hodgson and J. R. Robinson have studied forty-one patients with traumatic and surgical wounds treated by sulphanilamide applied locally. It was observed that many of these patients seemed to be worse after operation than were others not treated by sulphanilamide, and in some cases toxic symptoms occurred. To measure the amount of absorption which took place, the free sulphanilamide concentration in the blood was estimated at intervals by Werner's colorimetric method; readings were made every six or eight hours for twenty-four hours, then twelve-hourly and finally daily. The curves obtained were of a characteristic shape suggesting rapid absorption and slow excretion. The highest concentration was found to exist at about twenty-four hours, and was usually of the order of 1 milligram per 100 cubic centimetres for each gramme (15 grains) of sulphanilamide placed in the wound. Absorption was highest from muscle tissue with good circulation. The wounds appeared to heal slightly more slowly than when sulphanilamide was not used, but infection was well controlled except in two cases in which gas gangrene supervened.

Treatment

Effects of wearing crash helmets.—The value of an efficient crash helmet in mitigating the effects of head injuries in motor cyclists is shown by a series of cases reported by H. Cairns and H. Holbourn. Two main types of helmet are in use. The first consists of an outer shell made mainly of hard vulcanized rubber and an inner suspension system connected to the shell by means of a stout cord. If this cord breaks nothing prevents the rider's head from coming into contact with the outer shell. In the second type, which gives better results, the outer shell is made of compressed wood pulp and the inner slings are stitched separately to the outer shell. The patients fall into three groups as follows. (1) Those who die before they can be removed to hospital. (2) Those who are so slightly injured that they are not taken to hospital or if taken to hospital are not detained; (3) Those admitted to hospital. Information about the first two groups is meagre. Of the hospital cases, numbering 280, seventy-two were wearing crash helmets. Of fifty-five patients admitted in the acute stage twenty-two were wearing crash helmets and among them the incidence of fracture of the skull was 32 per cent. Among the thirty-three not wearing crash helmets the incidence of fracture was 63 per cent. The incidence of fracture among the patients admitted in the subacute or chronic stage was 39 per cent for those without and 40 per cent for those with crash helmets. This may be

accounted for by the fact that the marks on the helmet are helpful in enabling a late fracture to be found by means of radiographical examinations. Fractures which do occur when a pulp crash helmet is worn tend to be less severe. The incidence of prolonged amnesia (one day or more) is only one-third of that associated with accidents in which a crash helmet is not worn. Serious intracranial complications are greatly reduced in frequency, and in non-lethal accidents it is estimated that the pulp crash helmet so reduces the severity of the injury that the proportion of motor cyclists requiring hospital treatment is reduced by one-half.

Essentials of first aid

Need for simplification.—Simplification of the conventional teaching of first aid is, as a Leading Article (1942¹) in the *Lancet* says, a war-time desideratum. General agreement has been reached about the principles to be taught, although details may vary. Thus the first step on reaching a casualty is to protect him as far as possible from any source of danger such as moving machinery or tottering masonry. The next step is to stop bleeding by firm application of dry dressings. Tourniquets are seldom necessary and most authorities agree that they should be reserved for cases of traumatic amputation. Pressure points have taken a less prominent place in teaching than they formerly occupied. The mouth must next be cleared of rubble and dust and artificial respiration given if necessary, especially if coal gas poisoning is suspected. Cleansing of wounds is not advised, because it is usually impossible at the scene of the accident and always wastes time. Splinting is reduced to a minimum, to save time and to lessen handling. A fractured patella should always be splinted but other fractures of the limbs are treated by tying the legs together or bandaging the arm to the trunk. Burns should be covered with a dry dressing and the patient got away to hospital as quickly as possible. Blanketing and lifting should be carefully taught. First-aid workers must be taught to assess the gravity of a case so that when many patients have to be dealt with the worst injuries have priority. Doctors must take a full part in the teaching if this sense of proportion is to be acquired. The danger period is between the time of rescue and the time of arrival at hospital, and the good first-aid worker will see that this interval is reduced as much as possible according to the gravity of the case.

The morphine controversy

Limited administration advisable.—A Leading Article (1942²) in the *Lancet* calls attention to the gradual emergence of a more rational view of the proper use of morphine after injuries. Until lately large doses were almost a routine prescription for shock, and many patients received morphine who, in the words of the *Army Medical Department Bulletin* (October 1942), would have done better with a cup of tea. Pain and the restlessness resulting from anxiety or haemorrhage are the real indications for morphine. The smallest effective dose should be given, and if rapid action is desired $\frac{1}{2}$ to $\frac{3}{4}$ grain may be injected slowly into a vein. In shock morphine is theoretically of value in allaying restlessness and in lowering metabolism, thus reducing the oxygen needs of the less important tissues; but, it also depresses the respiratory centre and thus reduces oxygen intake. With the low blood pressure of shock the addition of morphine may be followed by stoppage of urinary secretion. Morphine also renders patients poikilothermic, so that they must be guarded against changes of temperature. In cases of head injury other sedatives, such as barbiturates, are preferable. Chest injuries treated with morphine are liable to be followed by collapse of the lung, and the more the patient moves, within limits, the better.

Wound toilet

Value of soap and water.—R. L. Kerrigan adopted five years ago, and has used in 12,044 cases, soap and water cleansing of accidental wounds. The procedure should be carried out at the earliest possible moment and with the utmost care and thoroughness. It requires patience but the time spent is likely to be well repaid. The wound is first covered with a sterile dressing and the skin around it is cleansed. For this purpose grease solvents may be used, but the final washing is done with a neutral white soap solution and with pledgets of sterile cotton-wool. The skin edges are then covered with sterile cloths and the wound itself is cleansed thoroughly. Clots, foreign bodies and devitalized tissue are removed first and the whole surface is washed with the soap solution and finally rinsed with saline run through a catheter into all the recesses of the wound. Packing is applied and the whole surrounding area and the table underneath are dried as much as possible, to avoid any contamination through capillarity, before fresh towels are put on; then the surgeon, having changed his gown and gloves, proceeds to carry out any further operative treatment which may be required. In the present series of cases it was necessary in only eighteen instances (0.14 per cent) to keep the patients in hospital because of the subsequent development of infection. It is clear, however, that the injuries must have been of a comparatively minor character since all the patients were treated in the first instance as out-patients.

Crush injuries

Clinical picture

Low blood pressure and anuria.—M. Grace Eggleton, K. C. Richardson, H. O. Schild and F. R. Winton have carried out experiments in which crushing injuries were inflicted on twenty anaesthetized dogs by compressing one limb for periods of from four to five hours. Release of pressure was invariably followed by a sharp fall of arterial pressure and oliguria or anuria. When any urine was secreted it was deeply pigmented, presumably with

myohaemoglobin, and the creatinine clearance was very low. The flow of urine could be restored to normal by intravenous infusions and diuretics, but the creatinine clearance, that is the concentrating power of the kidney, recovered to only about one-quarter of its original value. That damage to the kidney is not caused by low arterial pressure *per se* is shown by the fact that an even greater lowering of the blood pressure by histamine infusion does not affect the creatinine clearance rate. Characteristic changes were found *post mortem* in the kidneys; the cortex was brown, the medulla was of a bluish pink colour, and a narrow light-coloured zone often separated the two. The organ was notably flaccid. Microscopically the lumina of the tubules contained material which might have caused some degree of blocking, but no relation was found between the amount of the deposit and the degree of functional impairment. Blockage should, moreover, produce a tense kidney. The authors consider it most likely that a poison released from the crushed limb damages the tubule cells, increasing their permeability to creatinine and other substances which are concentrated by the kidney, and thus enabling such substances to diffuse back into the blood stream. Hastening the flow of urine down the tubules would impede the process of reabsorption, and would account for the partial recovery in the creatinine clearance which was observed when the arterial pressure was raised and diuresis induced by treatment.

Treatment

By pressure — As a Leading Article in the *British Medical Journal* points out, rational treatment of the 'crush syndrome' is impossible while its pathogenesis remains obscure. The two main views are (1) that shock and renal damage result from the same lesion, namely muscular necrosis, shock being due to escape of plasma from the blood stream into the injured tissues, renal damage to its subsequent reabsorption, the plasma being more and more laden with toxic bodies as circulation improves; (2) that loss of blood constituents into the damaged limb accounts *per se* for both shock and renal damage. D. H. Patey and J. D. Robertson, who hold the second view, have successfully treated two patients by the application of intermittent positive pressure up to 60 millimetres Hg, using a specially made large blood pressure cuff and a pavaex motor, and they now suggest that the same principle be applied in first-aid treatment of these cases. The method recommended is to bandage the limb firmly from below upwards with a 3-inch elastic web bandage stretched to double its unstretched length, with each turn overlapping the one below. The bandage is marked in half inches, so that the required degree of tension can easily be estimated by the eye. First-aid parties should be taught to apply such a bandage immediately the limb has been released from pressure. The leading article above referred to emphasizes the danger that in inexperienced hands the bandage might be applied too tightly and cause or increase circulatory obstruction, possibly ending in gangrene of the limb. Intermittent application of positive and negative pressure might, moreover, increase absorption from the damaged area and injury to the kidneys, supposing that the toxic theory is correct. Further experimental and clinical evidence is urgently required.

Experimental results in dogs — G. W. Duncan and A. Blalock have studied experimentally the effects of crush injury in animals. The thigh of an anaesthetized dog was crushed in a press for five hours. The authors have shown previously that very few animals recover from such an injury, the average survival time being about seven and a half hours, but that some can be saved by placing the limb in a pneumatic tube exerting a pressure of 40 millimetres Hg immediately after removal of the limb from the press. One of the chief objects of the present experiments was to prolong life sufficiently to allow observations to be made during the later period, corresponding to that in which oliguria and uraemia have developed in some of the human cases of crush injury. In fifteen animals intravenous infusion of plasma was begun immediately after removal of the press, the quantity to be injected was estimated by measuring the fluid loss into the injured area in untreated animals. An additional loss equivalent to almost two-thirds of the amount injected was observed in the plasma-treated animals. Nine of the animals died, the average survival time being twenty hours. In the remaining six, swelling of the limb, shock, oliguria, haematuria and casts in the urine, corresponding to similar changes observed in human beings, appeared after removal of the press but late development of oliguria, cylindruria and uraemia followed by death with characteristic changes in the kidneys such as have been seen in human beings after crush injuries, did not occur. The urinary output had increased to normal by the end of forty-eight hours and remained normal afterwards. Urinary creatine and creatinine were raised at first, but had returned to normal limits within forty-eight hours and did not show any late rise. The non-protein nitrogen of the blood rose immediately, but by the end of the fourth day normal levels were recorded in all the animals. Transient elevations of the non-protein nitrogen were observed in all animals during the succeeding period (at least forty days, except in one animal which died on the twenty-third day) of observation. The effect of cooling was tested in nineteen animals. In seven, the limb was kept surrounded by ice all the time that it was in the press; in twelve, cold was applied after removal of the press which had been kept in position in six cases for five hours, in six for three and a half hours. The maintenance of a low temperature during crushing appeared to exert a protective influence; five of the animals lived for at least twenty-three days afterwards. The urinary output was less reduced than in either untreated animals or those treated with plasma; naked eye haematuria occurred in only two of the five, urinary creatine and creatinine were hardly raised and blood changes were minimal. Cooling of the limb after removal of the press, on the other hand, did not have any protective effect.

Experiments with refrigeration.—A. Blalock describes a series of twenty experiments designed to demonstrate the influence of cooling upon an injured leg to which a tourniquet has been applied. Large animals were used. Pain was prevented by narcotics. Injury was caused by repeatedly striking the limb with a blunt instrument for five to eight minutes. As soon as this had been done a tourniquet was placed upon the thigh and the limb was packed round with ice. The tourniquet was left in place for five hours. In ten of the animals intravenous administration of plasma was begun as soon as the tourniquet was removed. The limb was kept in ice for six hours after removal of the tourniquet. The rectal temperature fell considerably in all cases, especially after the tourniquet had been removed. The deleterious effect of a tourniquet upon an injured limb has previously been demonstrated by the author. In ten experiments in which a limb was subjected to injury of a similar kind, in which plasma was given and in which a tourniquet was not applied, all the animals recovered. In ten experiments in which a tourniquet was applied to the injured limb for five hours all the animals died. In the present series of experiments, of the ten animals given plasma, five recovered and of the ten not given plasma, four recovered, in other words cooling greatly reduced the mortality resulting from application of a tourniquet to an injured limb and the effect of cooling was enhanced by infusion of plasma to compensate for loss of fluid into the injured part.

Blows

Clinical picture

Cardiac injuries—L. H. Sigler draws attention to the possibility of damage to the heart and adjoining structures resulting from non-penetrating injuries and stresses. Animal experiments have shown that death may occur in such cases without structural damage to the heart being detectable *post mortem*. The types of trauma which may cause cardiac injuries in man are blows on the chest, especially in the praecordial region; antero-posterior compression of the chest; extreme increase of intra-abdominal pressure by external violence; lifting an extremely heavy object; disturbance of vagosympathetic innervation produced by direct injury or reflexly. Structural damage may be found in the pericardium, myocardium, coronary vessels, valves and great vessels, and in the lungs and pleurae. More than one of the above structures may be involved. In some cases of death from cardiac arrest, necropsy—as in some of the experimental animals—does not show any structural damage. Late effects of cardiac injury in the shape of ventricular aneurysm and calcification of the heart and pericardium may be observed long after the injury. Injuries to the heart may not produce any symptoms or signs, but in most cases after the initial injury dizziness or unconsciousness develops immediately or after a short period. The patient usually recovers quickly (except in fatal cases, when death occurs without recovery of consciousness) but may subsequently complain of epigastric or praecordial discomfort, or of mild pain. Several hours or days later a typical anginal syndrome may develop, usually precipitated by excitement or exertion, and the attacks may continue to recur for months or years. In other cases dyspnoea occurs, or the patient may complain of cough, palpitation or 'fluttering', weakness, nausea or vomiting. Signs of circulatory collapse may appear soon after the accident; later, rise of temperature, of the leucocyte count and of the erythrocyte sedimentation rate may be observed. The area of cardiac dullness and the cardiac shadow in the X-ray film may remain normal or may be enlarged as a result of cardiac dilatation or pericardial effusion. The first sound may be diminished, and gallop rhythm may occur. Pericardial friction may be audible and endocardial murmurs may develop, especially if valvular damage has occurred. Arrhythmias of various kinds (ectopic contractions, auricular fibrillation or flutter, or irregularities due to heart block) may be observed. Abnormalities may appear in the electrocardiogram and are usually progressive; they are possibly due to infarction of the myocardium. The diagnosis is based upon the history and symptoms, upon the absence of previous heart disease and upon the clinical, radiological and electrocardiographical findings.

Blast injuries

Pathology and morbid anatomy

Blast injury to the lungs.—In order to test the validity of the theory that blast injury to the lungs is due in part at least to the low-pressure phase, A. L. Latner has investigated the effect on mice of exposure to low pressures of short duration by means of a vacuum chamber. Death occurred instantaneously or almost at once in about half the animals, and at necropsy haemorrhagic lesions were found constantly in the lungs and less regularly in extrathoracic organs. The mice which recovered were killed at varying intervals and the recovery process was studied; the appearances were identical with those observed in human subjects with blast injury. The author suggests that low pressure acts by producing an extreme difference between intrapulmonary and extrapulmonary pressure, with consequent overinflation of the lungs and tearing of capillaries. On such a hypothesis a tight bandage or jacket should be useful in the prophylaxis and treatment of blast injury to the lungs.

EDITORIAL COMMENTARY—Modern Wound Treatment

War-time conditions afford an exceptional opportunity for the intensive study of wound treatment and it is now possible to assess the value of new methods which have been tried out during the past three years.

It can be confidently stated that the basic principle of prophylactic wound treatment established in 1917–18 has been found sound. This principle was the surgical excision of the wound

(debridement or épiluchage) as soon after the infliction of the injury as possible. Recent experience has shown that wide excision of the skin is unnecessary and has emphasized the importance of free excision opening of the fascia even when anatomical details render a full excision inadvisable. The time lag, after which the procedure loses its value or may prove dangerous in stirring up established infection, has been variously estimated. Most authorities put it at twelve hours; there is no doubt, however, that in well-vascularized areas such as the face and the scalp the procedure may be valuable up to two or three days. It is probable that the use of sulphonamides by the mouth and locally have assisted in the extension of the safe period. Experience in the Army has confirmed the condemnation of primary suture after wound excision. In dealing with air-raid casualties surgical interference is often possible at a much earlier stage after injury, and primary suture under such circumstances may often prove successful although it always involves the risk of the later development of a deep anaerobic infection which may be disastrous if it is not recognized early. The question of primary suture of the flaps after amputations is answered on similar lines. From a practical point of view, if the surgeon is in doubt, it is always better to avoid the use of sutures in potentially contaminated wounds; the only exception to this advice is in the case of head wounds involving the brain. It should be remembered that if a wound remains infected to a serious degree, secondary suture and skin grafting can make good most defects with little lengthening of the period of convalescence.

Current interest has concentrated mainly on the use and value of the sulphonamide group of drugs in the prophylaxis and treatment of wounds. Enthusiasm over their merit should not blind us to their limitations or encourage us to neglect timely surgery. The opinion is held generally that sulphanilamide given orally and lightly packed into the wound has reduced the incidence of serious streptococcal infections and possibly those due to some anaerobes. It must be said that as yet no convincing control experiments on man have been recorded to prove this opinion. However, the experimental evidence in laboratory animals, and the fact that the administration, if due regard to dosage is given, has been innocuous, encourage us to continue the use of this prophylactic. Up to date sulphanilamide usually has been employed. Sulphathiazole is on trial and in view of its bacteriostatic action on the staphylococci as well as on the streptococci, it may prove the more satisfactory agent.

In treating established infections, although the sulphonamide group have their place other chemicals of a more definitely antiseptic action are on trial. Penicillin and propamidine are the most interesting of them, but both are still available only in experimental quantities, and a final judgment of their value must await the results of further experience.

The treatment of anaerobic infections such as tetanus and gas gangrene, which are little thought of in peace-time, are major problems under war conditions. The prophylactic use of tetanus toxoid in the British and American Armies has proved its great value. As a whole the incidence of tetanus has been small up to date and among the inoculated much rarer and less severe than in those who have not received the prophylactic injections. The use of antitetanic serum (two or three doses of 3,000 units) is still recommended for all contaminated wounds to protect those in whom the toxoid injection may be lacking or ineffective. Infections classified as gas gangrene have been rare in the present war in comparison with those in the last, but if they become established they carry a high mortality. Prophylactic injection against them is still in the experimental stage. The use of antiserums is advised in treatment although experience has made it clear that surgical wound excision is still our sheet-anchor in checking disasters. The value of the sulphonamide group of drugs in combating gas gangrene infections is supported by animal experiment, especially with sulphapyridine, but there is no convincing evidence of their effectiveness in man. X-ray therapy has been advocated for the treatment of gas gangrene but can hardly be expected to check an intense destructive inflammatory process. It has been shown that anaerobes are present in many if not in most contaminated wounds without leading to progressive gangrene or to serious toxic effects, and in such cases many measures may appear to effect a cure on a bacteriological basis.

In the treatment of established wounds attention has always been directed to the discovery of an application which tends to expedite the healing process. It is doubtful if such stimulation is of much value. It would appear that convalescence can be more effectively expedited by the timely use of skin grafts and by the avoidance of the use of any chemical which can depress normal wound reaction.—C. MAX PAGE.

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INTESTINAL OBSTRUCTION

See also B.E.M.P., Vol. VII, p. 221; and Cumulative Supplement, Key Nos. 761–775.

Acute intestinal obstruction

General treatment

Importance of Miller-Abbott tube.—B. C. Smith and F. T. van Beuren analyse 130 cases of acute intestinal obstruction in a paper read before the New York Surgical Society. The cases fall into six four-year periods, wherein the percentage mortality rates were as follows: 66.6, 53.7, 44.4, 48.6, 28.4 and 23.8. The drop in mortality in later periods is attributed to earlier diagnosis; adequate replacement of fluid and electrolytes; better anaesthesia; the use of peristaltic drugs and rectal treatments; the sulphonamide drugs; and especially the employment of the Miller-Abbott tube and gastric suction. The operative treatment varied according to the necessities of the case from division of a band to resection of small or large intestine. Enterostomy has been less frequently performed since the advent of the Miller-Abbott tube. Spinal anaesthesia is preferred because it reduces distension of the bowel, giving better exposure and easier closure. The mortality is about 2 per cent lower when spinal or local anaesthesia is used than when general anaesthesia is used. Disadvantages are fall in blood pressure, anoxaemia and shock, necessitating the use of ephedrine, intravenous infusions and oxygen. Local anaesthesia was reserved for the most seriously ill patients. X-ray examinations were made in 83 cases, with positive findings in 94 per cent. A negative X-ray should never be allowed to weigh against a positive clinical diagnosis but a positive X-ray is valuable confirmatory evidence of obstruction. The Miller-Abbott tube was used in thirty-six cases. It is passed as far as the pylorus after the nose and pharynx have been cocaineized and its progress into the duodenum is watched on the fluorescent screen. Once in the duodenum the bag is blown up and the tube is allowed to progress of its own accord. Meanwhile continuous gastric suction is employed. The use of the tube may obviate the need for emergency operation in an early case and it is very valuable as a pre-operative measure in late cases. Its use after resection of a growth of the large bowel has largely replaced enterostomy as a decompressing procedure and has enabled a larger number of successful one-stage operations to be carried out.

Obstruction of the small intestine

Leiomyosarcoma of the small intestine

Microscopical findings.—J. A. Rankine reports, with a useful commentary, especially on the question whether these rare tumours, the leiomyosarcomas, are malignant from the start or whether they are innocent and subsequently undergo malignant change. The usual site is the upper part of the small intestine, but three cases have been recorded in Meckel's diverticulum. The tumours are of two kinds: (1) submucous, suggested by Demel as arising from the muscularis mucosae and (2) subserous, the less rare; out of Rankine's eighteen collected cases thirteen were subserous and five were submucous. The subserous growths have been thought to arise from the muscularis propria (Demel). Microscopically, the differential diagnosis between spindle-celled sarcoma, cellular fibroma and malignant leiomyosarcoma may be made on the following criteria: (1) fibrous tissue may show abnormal new growth, but fibroblasts predominate here forming a sarcoma; (2) muscle cells are sharp in outline with definitely pointed extremities, whereas fibroblasts have ends breaking up into an arborization of fine tendrils; (3) the nuclei of muscle cells are more numerous, have rounded ends and lie within the cell bodies; nuclei of fibroblasts, on the other hand, are less numerous, spindle-shaped and shorter, and they lie on the surface of the cell body; (4) muscle cells do not show any of the many striations characteristic of fibrous tissue. Grossly the tumours are pale white to pink, hard, coarse, nodular, rather non-vascular, prone to degenerate in the centre and form cysts. Other degenerate changes are fatty, hyaline and necrotic in type; calcification may also occur. Ulceration of the overlying mucous membrane occurred in seven out of nineteen cases; in seven out of twenty-one cases there were metastases. The complications that may occur are ulceration with haemorrhage and anaemia, intestinal obstruction due to intussusception, adhesions and perforation of the intestine. Correct pre-operative diagnosis was made in six out of twenty-two cases. Men are more often affected (in thirteen out of nineteen); the most frequent age period is from thirty to fifty.

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Smith, B. C., and van Beuren, F. T. (1943) *Ann. Surg.*, **117**, 427.

JAUNDICE

See also B.E.M.P., Vol. VII, p. 261; and Cumulative Supplement, Key Nos. 779–788.

Classification of jaundice

Jaundice in the Tropics

As complication of tropical diseases.—P. Manson-Bahr, dealing with jaundice in the Tropics, describes the following types. (1) In malaria jaundice is a frequent concomitant of the subtertian or malignant form, and results from haemolysis. Recurrent urobilinuria is a valuable clinical sign. In severe infections with *Plasmodium falciparum* toxic jaundice may occur as the result of focal necrosis of the liver. Similar toxic jaundice characterizes blackwater fever. Excessive secretion of bile in subtertian malaria is sometimes succeeded by obstructive jaundice due to the formation of pigmented calculi. (2) Haemolysis similar to that of malaria occurs in Oroya fever, caused by the intracellular parasite *Bartonella bacilliformis*. (3) Jaundice has been reported in connexion with both acute and chronic kala-azar. The pathogenesis of the acute cases is unknown; in the chronic cases cirrhotic changes occur in the liver. (4) Both louse-borne and tick-borne relapsing fever may be associated with haemolytic jaundice. In severe epidemics of *Spirochaeta recurrentis* and *Spirochaeta duttoni* infection, deep jaundice due to focal necrosis of the liver has been observed. (5) In Weil's disease the jaundice which develops in 74 per cent of cases may be so deep as to suggest carcinoma of the liver. It is a true bilirubinaemia associated with toxic necroses in the liver. (6) Yellow fever presents a partly haemolytic, partly toxic jaundice. Jaundice, sometimes fatal, has followed prophylactic immunization against yellow fever. (7) Jaundice in amoebiasis is rare but may occur as the result of pressure by an abscess in the quadrate lobe of the liver. (8) Non-alcoholic cirrhosis of the liver is widespread in the Tropics, especially in Southern China. The aetiology is obscure. Infective hepatitis is also common. Both give rise to the obstructive type of jaundice. (9) Other liver infections are sometimes associated with jaundice. Bilharziasis may show terminal jaundice; eggs are deposited in the liver and eventually produce fibrosis. Clonorchiasis, due to infestation of the bile ducts with *Clonorchis sinensis*, is associated with cirrhotic changes in the liver, sometimes terminating in cancer. Ascarides may invade the common bile duct. (10) Banti's disease and hepatic cancer are common in the Tropics. (11) Jaundice is sometimes a sequel to other infections, for example cholera and typhus.

Toxic and infective hepatic jaundice

Classification of cases

Causative agents reviewed.—R. Ottenberg and Rose Spiegel review the data relating to non-obstructive jaundice caused by infective or chemical agents. The cases may be classified as follows. (1) Infective forms of jaundice include, first, simple 'catarrhal' jaundice of unknown aetiology. The mode of onset varies in the different epidemics. The disease may start as an upper respiratory infection or as a gastro-intestinal disturbance. Clinical recovery is complete but residual impairment of liver function is occasionally revealed by tests. The aetiological agent is thought to be a virus. The virus may remain latent in the blood, which would explain the occurrence of jaundice after injection of measles serum. This form of jaundice appears to be related to acute infective liver atrophy, also probably due to virus infection. Several different viruses are thought to be involved. Secondly, leptospirosis (spirochaetal jaundice) includes a number of related diseases of which the classical instance is Weil's disease. At least four leptospirae can cause jaundice; some are carried by rats, others by dogs. Jaundice is often absent; it occurs in only 50 per cent of cases of Weil's disease and 2 per cent of cases of 'field fever'. Thirdly, yellow fever has been shown to be due to a virus which is readily grown on chick embryo tissue cultures. The serum of recovered patients exerts a protective action on inoculated white mice. Two great endemic reservoirs of the disease have been shown to exist, one in the Amazon basin and one in West Africa. The disease is kept alive in monkeys and possibly in other animals. Active immunization is the most effective prophylactic. Fourthly, systemic infections which may be associated with jaundice include lobar pneumonia and pneumococcal peritonitis, septicaemia, syphilis (congenital, secondary and tertiary), tuberculosis, acute infective mononucleosis and malaria. (2) The jaundice produced by chemical agents may be caused in one of three ways: by direct poisoning of the liver cells; by haemolysis, the products of which injure the liver cells, by reaction caused by idiosyncrasy. Allergy has not been proved to cause liver damage. The list of chemical agents is a long one. It includes inorganic compounds such as phosphorus, arsenic, bismuth and mercury; organic compounds such as chloroform and avertin; aromatic compounds, for example the arspenamines, sulphonamides and coal tar; biological substances such as incompatible blood and snake venom and so far as physical agents are concerned distilled water and burns may cause jaundice. The authors point out that jaundice as a complication of burns has appeared only since the introduction of tannic acid treatment, and may be related to it.

Manson-Bahr, P. (1943) *Practitioner*, 150, 265.

Ottenberg, R., and Spiegel, Rose (1943) *Medicine, Baltimore*, 22, 27.

JOINTS, DISEASES AND DISORDERS

See also B.E.M.P., Vol. VII, p. 278.

Pulmonary osteoarthropathy

Hypertrophic osteoarthropathy and clubbing

Pathogenesis.—The pathogenesis of finger and toe clubbing and of hypertrophic osteo-

arthropathy is discussed by M. Mendlowitz. In simple clubbing of a digit the enlargement is confined to the terminal segment; in hypertrophic osteoarthropathy the process extends proximally and is associated with deposition of newly formed periosteal bone and involvement of joints. Clubbing may be divided into three groups. (1) symmetrical, involving all four limbs; (2) unilateral, involving one limb; and (3) unidigital, involving only one finger. Hypertrophic osteoarthropathy may be associated with any of the three varieties or it may be apparently idiopathic. Symmetrical clubbing may be congenital (hereditary) or acquired. In the latter event it is most often associated with diseases of the lungs, pleurae or mediastinum, including suppurative conditions such as bronchiectasis and empyema, tuberculosis and atelectasis from bronchial obstruction. Sometimes the condition arises in connexion with cardiac lesions, including congenital heart disease and subacute endocarditis, in cirrhosis and other diseases of the liver, and in gastro-intestinal conditions associated mainly with chronic diarrhoea such as ulcerative colitis and bacillary dysentery. Isolated cases have been reported in association with other diseases, but the possibility of the unrecognized co-existence of one of the more common causes must be borne in mind. Unilateral clubbing is most often observed in cases of aneurysm of the aortic arch, or of the innominate or the subclavian artery, but it has occurred in connexion with lesions such as carcinoma of the apex of the lung and apical tuberculosis. Unilateral clubbing has developed after trauma to the finger and gout. Hypertrophic osteoarthropathy is found most often in cases of chronic pulmonary disease. Radiographic changes, consisting in expansion of the ungual part of the terminal phalanx and osteoporosis of the whole bone, appear in advanced cases of clubbing. Periosteal proliferation, affecting particularly the bones which are proximal to the phalanges, is seen in hypertrophic osteoarthropathy. Microscopically clubbing is characterized by proliferation of all the tissues of the finger tips. In hypertrophic osteoarthropathy deposition of new periosteal bone is associated with increased porosity which is the result of osteoclastic hyperactivity. Attempts to produce such changes in animals have met with but little success, but hypertrophic osteoarthropathy has been produced by anastomosis of the pulmonary artery to the left auricle, so that part of the ventricular output is diverted from the lung; this resulted in increased systemic cardiac output, the flow through the lungs remaining almost unchanged. In acquired symmetrical clubbing, increased digital arterial pressure and consequent increased blood flow have been observed; in hereditary clubbing and in hypertrophic osteoarthropathy such changes were absent and in unilateral clubbing they were variable. The author believes that whatever may be responsible for clubbing and for hypertrophic osteoarthropathy, increased peripheral circulation plays an important part.

Mendlowitz, M. (1942) *Medicine, Baltimore*, **21**, 269

KELOID

See also B.F.M.P., Vol. VII, p. 366

Aetiology

Causation

Causes and treatment. - J. Garb and M. J. Stone describe a series of eighty cases of keloid and review the literature. Although trauma is probably always the direct cause of keloid, it is sometimes so trivial that it passes unnoticed and the consequent keloid may then be dubbed 'spontaneous'. Keloid may arise in the scars of acne, herpes and other similar lesions. In 67 per cent of the eighty patients the keloid was situated in the upper half of the body. The chief disposing factors are age and race, most cases occurring between the ages of ten and twenty, and keloids being particularly common in negroes, Hindus and Malaysians. A familial disposition is occasionally noted. No evidence was obtained that syphilis or tuberculosis is an aetiological factor. It is considered likely that hormonal factors play an important part but concerning the gland or glands involved the evidence is conflicting. Keloids are distinguished from hypertrophic scars by the fact that they tend to extend, usually in a claw-like fashion, beyond the bounds of the original injury. Sarcoids, scleroderma and fibromas show a distinctive microscopic structure. Paraffinomas have a characteristic microscopic appearance and are associated with a history of paraffin injections. Irradiation by X-rays or radium is the only effective treatment; older and larger keloids usually require a bigger dosage than smaller and younger growths. Surgical excision alone is invariably followed by recurrence; it may be used for very large keloids if irradiation at the first sign of recurrence is also given. Of the many other forms of treatment suggested, none is of the least use.

Garb, J., and Stone, M. J. (1942) *Amer. J. Surg. N.S.*, **58**, 315

KIDNEY, SURGICAL DISEASES

See also B.E.M.P., Vol. VII, p. 380; and Cumulative Supplement, Key Nos. 829-840

Hydronephrosis

Treatment

Preliminary nephrostomy.—The size of a hydronephrosis tends to be limited by the super-vention, sooner or later, of infection with consequent thickening of the wall, and sacs of over 1,000 cubic centimetre capacity are rare. F. Lieberthal reports such a case in a girl, aged three and a half years. A symptomless abdominal swelling had been present since the age of

eight months; when the child was first seen a cystic mass was found to occupy the whole of the right and part of the left side of the abdomen, extending above the costal margin and down into the pelvis. The blood pressure was 140/80 millimetres Hg. Physical examination was otherwise negative and the urine was normal. Intravenous urography showed a normal left kidney and absence of excretion by the right kidney. Transvesical urography with injection of 300 cubic centimetres of hippuran (sodium ortho-iodohippurate) solution revealed a globular shadow filling the abdomen. The right ureter was pushed considerably over to the left side. The patient subsequently had a severe reaction, the temperature rising to 105° F. Nephrostomy was performed and 2,700 cubic centimetres of fluid was aspirated. The temperature fell, and ten days later the kidney was removed. The sac measured 22.5 × 12.5 × 12.0 centimetres, and the renal substance was 3 millimetres thick; the capacity was 1,000 cubic centimetres, proof that preliminary nephrostomy produces shrinkage and facilitates nephrectomy.

Calculi

Aetiology

Anuria after sulphapyridine.—A case of anuria, due to sulphapyridine administration, in which ureteric drainage was successful is reported by R. C. S. Benson and R. C. Percival. A man, aged thirty-eight, with broncho-pneumonia, had been treated by sulphapyridine, of which 21 grammes (315 grains) was given in three days. After this time his chest condition was progressing satisfactorily and sulphapyridine was stopped. Thirty-six hours later he suddenly experienced pain in the penis and passed a small quantity of blood-stained urine. He was admitted to hospital six hours afterwards. Extreme tenderness was present in both loins, especially in the right. Catheterization yielded one ounce of almost pure blood. Intravenous infusion of sodium citrate solution was started. Fluid given by mouth was vomited. Thirty hours later urine had not been passed and the general condition had deteriorated. Cystoscopy was then performed; the trigone of the bladder showed submucous haemorrhages and small deposits of crystalline debris. Both ureteric orifices were oedematous; on the left side the catheter entered with difficulty for the first five centimetres but easily passed afterwards. On the right side the ureteric orifice was completely blocked by a plug of debris, but after this had been dislodged the catheter passed easily. Dark amber-coloured urine escaped from both catheters, which were left in place. The debris from the bladder contained many sulphapyridine crystals; none was found in the catheter specimens. The urinary output for the next twelve hours was twenty-three ounces of blood-stained urine. Haematuria ceased after ninety-six hours. Six days later cystoscopy showed great improvement in the bladder, ureteric catheters passed easily and dye excretion was normal.

Tuberculosis

Pathology and morbid anatomy

Significance of tubercle bacilli in the urine.—W. H. Ordway and E. M. Medlar have endeavoured to solve the question whether or not tubercle bacilli in the urine are necessarily a sign of urogenital tuberculosis, by collecting over a period of ten years data relating to 287 patients with clinically active pulmonary tuberculosis and to 112 patients without evidence of pulmonary tuberculosis or with pulmonary lesions considered to be without clinical significance. Examination of the urinary sediment and guinea-pig inoculations were the methods used to detect tubercle bacilli. Of the tuberculous patients, twenty-two (7.7 per cent) had tubercle bacilli in the urine, but clinical evidence of urogenital tuberculosis was found only in five (22.7 per cent) of these. Thirty-three patients died, of whom four had been shown to have tubercle bacilli in the urine. Necropsy was performed in thirteen cases and tuberculous lesions of the kidney were found in four; of these four, one only had shown tuberculous bacilluria. Among the second group of patients (with pulmonary lesions absent or inactive) bacilluria was observed in eleven patients; seven of these had been sent to hospital with a diagnosis of renal tuberculosis, having undergone nephrectomy; of the remaining four, nephrectomy was performed in one case. The total number of cases of bacilluria, therefore, was thirty-three; nephrectomy was performed in eight, and renal tuberculosis was proved. Five patients died, and three necropsies were done, renal tuberculosis being found each time. Of the remaining twenty patients, eighteen have not shown as yet any evidence of progressive renal tuberculosis, and two have signs of bilateral renal lesions. The above findings are held to indicate that the presence of tubercle bacilli in the urine is not necessarily a sign that progressive renal tuberculosis is present, and that surgical intervention should be withheld until evidence of renal involvement is manifest. The length of time for which each patient was observed subsequently is not stated.

Tumours

Clinical picture

Adenocarcinoma of the kidney complicating pregnancy.—Six cases of malignant renal tumour complicating pregnancy have been reported in the literature and these are reviewed, and a further case is described by A. E. Vitt and W. F. Melick. Their patient, aged twenty-one, was well throughout her pregnancy and the blood pressure remained normal. On one occasion, at the third month, haematuria was detected by microscopy but treatment was not given; as a result of this omission, as the authors point out, several months' valuable time was lost. Three months after delivery the patient had an attack of haematuria and of pain in the back.

Physical examination was negative. Cystoscopy showed bleeding from the left kidney and on the left side slight delay in the excretion of phenolphthalein. Retrograde pyelography showed a filling defect of the left renal pelvis and lower calyces. Nephrectomy was performed and a papillary adenocarcinoma was found occupying the entire renal pelvis and apparently arising from the renal pelvic epithelium. Post-operative radiotherapy was given. The patient was well eighteen months after operation. The authors draw attention to the graver prognosis associated with the comparative youth of pregnant patients, but they cannot find any evidence that pregnancy *per se* adversely influences the outlook. Operation during pregnancy does not usually have abortion in its wake and it should never be delayed.

Nephrectomy

Prognosis

Conditions eight years after operation.—A paper on life after nephrectomy, based on a study of 156 patients, was read before the Section on Urology of the American Medical Association by H. L. Kretschmer. The patients were those who presented themselves for examination at the author's request eight years and two months on the average after nephrectomy had been performed for various lesions. Pain in the remaining kidney was complained of by seven of the patients; in three a lesion of the kidney was present. The incidence of cardiac enlargement was no greater than what would be expected in a similar age group of people possessing both kidneys. Blood pressure had risen since the operation in fourteen cases, but only two patients with hypertension were under fifty years of age. In six cases the blood pressure had fallen slightly since the operation. Non-protein nitrogen estimations were carried out in 146 cases. The values were found to have risen since the operation in 15 per cent. The Newburgh concentration test was done on 126 patients, 73 per cent of whom passed. Scoliosis was observed in eighteen patients, in three of whom it was known to have been absent before operation. Of the forty-nine patients on whom nephrectomy had been performed for tuberculosis five had X-ray evidence of tuberculosis in the remaining kidney and in eleven the urine was infected.

Benson, R. C. S., and Percival, R. C. (1942) *Lancet*, 2, 360.

Kretschmer, H. L. (1943) *J. Amer. med. Ass.*, 121, 473.

Lieberthal, F. (1942) *J. Urol.*, 48, 23.

Ordway, W. H., and Medlar, E. M. (1942) *J. Amer. med. Ass.*, 119, 937.

Vitt, A. E., and Melick, W. F. (1942) *J. Urol.*, 48, 601.

LABOUR: RUPTURE OF THE UTERUS

See also B E M.P., Vol. VII, p. 516.

During labour

Aetiology

General review.—F. E. Whitacre and L. Y. Fang review forty-four cases of rupture of the uterus treated during a seven-year period at the Peiping Union Medical College Hospital. The incidence was 1 in 220 of all the obstetric admissions to the hospital. The mortality rate in such cases has decreased year by year, a fact which the authors attribute to several factors, including improved facilities for blood transfusion, uniformity in the surgical management of the cases, advances in chemotherapy and the use—when indicated—of continuous suction to secure decompression of the gastro-intestinal tract. In the whole series twenty-five patients died, a mortality of 56·8 per cent. Only three of the infants lived, giving a foetal mortality of 93·1 per cent. The ages of the mothers varied from nineteen to forty-three years; only two were primiparæ. In thirty-eight cases the rupture was complete, in six incomplete. One rupture occurred before and forty-three during labour. Of the complete ruptures, thirteen occurred transversely through the anterior wall of the uterus, eleven through the left wall, eight through the right wall, three through the fundus and three through a classical Caesarean scar. Of the partial ruptures, five were in the lower uterine segment and one was in the fundus. The rupture which occurred before labour, and which was associated with the signs of concealed hæmorrhage, was thought to be caused by a ruptured varix. Of the other cases, twenty-four were due to maternal and nineteen to foetal causes. In the former group, contracted pelvis accounted for twelve cases, trauma for four; a Caesarean scar ruptured in three cases, the horn of a bicornuate uterus in one and in four no cause could be assigned. In the latter group, the causes were transverse presentation in nine, compound presentation in two, persistent occipito-posterior position in one; excessive size, hydrocephalus or tumour of the foetus in seven. For incomplete rupture the treatment advocated is repair from below and packing whenever possible; for complete rupture, or incomplete rupture associated with an adjacent hæmatoma, supravaginal hysterectomy with transvaginal drainage should be performed. Preliminary treatment for shock and bleeding is required. Packing from below is sometimes useful to control hæmorrhage temporarily.

• Whitacre, F. E., and Fang, L. Y. (1942) *Arch. Surg., Chicago*, 45, 213.

LABOUR: COMPLICATIONS OF THE THIRD STAGE

See also B.E.M.P., Vol. VII, p. 523.

Inversion of uterus

Treatment

Conservative treatment.—The advantages of conservative treatment of acute puerperal inversion of the uterus are emphasized by C. E. McLennan and J. L. McKelvey, who have treated four cases, one of which was fatal. The dangers are, in the early stages shock and loss of blood, in the later stages sepsis. Treatment should be directed against such complications, and the replacement or removal of the uterus may be left until later, when the patient has recovered from the acute stage. In patients who are not shocked one gentle attempt at manual replacement may be permissible; in general, however, it is better not to undertake any local treatment unless bleeding continues, when the vagina should be packed. The placenta may be left in situ if it is not already delivered. Multiple transfusions should be given, using whole blood if it is immediately available, otherwise plasma or serum is used. Care must be taken to avoid iso-immunization reactions associated with the Rh factor. To combat infection the vagina may be packed with gauze soaked in acriflavine and systemic sulphonamide therapy should be started at once. After from four to six weeks when infection has subsided, the uterus which is by now well involuted may be replaced surgically or removed. In rare instances spontaneous restoration may take place during the period of waiting.

Pulmonary embolism

Thrombosis and embolism in obstetrics and gynaecology

A general review — T. Koller discusses the problem of thrombosis and embolism in obstetrics and gynaecology. In a series of 494 deliveries the incidence of fatal pulmonary embolism was 1.4 per cent. The incidence of thrombosis and embolism in general was increased by any interference for spontaneous deliveries it was 1.0 per cent, after any vaginal operative procedure 2.6 per cent and after Caesarean section 7.2 per cent. Among 394 gynaecological cases the frequency of fatal embolism was 12 per cent, and it made no difference whether a major operation had been performed or whether the patient had merely been given radium treatment. In this group of patients predisposing factors appeared to be (1) age over forty years, (2) the presence of infection as shown by a high pre-operative sedimentation rate, (3) malignant or fibroid tumours, (4) cardiac or vascular disease including varicose veins, (5) adiposity and (6) pregnancy. Weather conditions are suspected as influencing the occurrence of thrombosis and embolism. In a series of twenty-four patients investigated from this point of view 80 per cent of the cases occurred in groups of three or more during periods of cold wet windy weather. For some years the author has instituted the following prophylactic treatment before and after operation: movement in bed, massage, early getting up, abundant fluids and an alkaline diet, that is one consisting mainly of fruit and vegetables. Predisposed patients, in addition, are nursed with the foot of the bed raised. The incidence of thrombosis and embolism has been considerably lower since 1938 when these measures were introduced.

Koller, T. (1943) *Schweiz. med. Wschr.*, **73**, 85

McLennan, C. E., and McKelvey, J. L. (1942) *J. Amer. med. Ass.*, **120**, 679.

LABOUR: OPERATIVE AND MANIPULATIVE PROCEDURES

See also B.E.M.P., Vol. VII, p. 533.

Induction of labour

Indications

Disproportion — A. B. Tamis and J. Clahr discuss the management of a first labour with an unengaged vertex presentation. Their conclusions are as follows (1) When the head can be made to engage, labour may be allowed to continue. (2) When the head overrides the symphysis pubis and cannot be made to engage, Caesarean section is the method of choice if the child is alive and normal. (3) When the head will not engage but overriding is not present, a trial of labour may be allowed; but if delivery fails to take place within twenty-four hours, extraperitoneal Caesarean section should be done if contra-indication does not exist.

Caesarean section

Classical operation

A series of 1,333 operations.—The experience of the Johns Hopkins Hospital with Caesarean section is the subject of a paper by C. P. Manahan, H. F. Connally, Jun. and N. J. Eastman. The series of 1,333 operations which they present is one of the largest ever recorded. Of these operations 781 were performed because of contracted pelvis and other forms of mechanical dystocia, 203 for toxæmia, 115 were repeat Caesarean sections, eighty-eight were performed for haemorrhage, forty for intercurrent disease and 106 were unclassified. The proportion of Caesarean sections to vaginal deliveries has risen considerably during the last decade, to 5.2 per cent in white and 5.9 per cent in negro women. The early operations included thirty-three vaginal Caesarean sections. These have been excluded from consideration because the vaginal route has been almost abandoned and because the conditions are different from those of an abdominal operation. Extraperitoneal operations have also been excluded on account of their small number (eleven). Cases of rupture of the uterus or in which the infant weighed less than 1,500 grammes have also been left out because the authors think that the problems presented by such cases differ from those of the ordinary Caesarean section. This leaves 1,333 operations to be considered, of which 67.1 per cent were of the classical type, 16.3

per cent were of the low cervical type and 16.6 per cent were Caesarean sections hysterectomy. During the last decade the percentage of low cervical section has risen to 20.0 and that of Caesarean section hysterectomy has fallen to 12.6. The percentage of Caesarean section for contracted pelvis has fallen during the past decade, especially among the cases with a diagonal conjugate of 100 to 109 millimetres. Despite the decline the still-birth and neonatal mortality rates among this group also show a dramatic fall. The factors believed to be responsible are (1) X-ray pelvimetry, which permits a more accurate estimation of the possibilities of vaginal delivery; (2) abandonment of test labour after twelve hours; (3) a study of the behaviour of the cervix. In cases of contracted pelvis of a degree incompatible with vaginal delivery the cervix seldom dilates satisfactorily. In test labours ending successfully dilatation usually nears completion in twelve hours. The number of Caesarean sections for pre-eclampsia has risen from 2 per cent in the first three decades to 7.8 in the last decade, the reason being the saving of delay effected. The maternal death rate for the whole series was 2.8 per cent. For negroes it was 3.5, for whites 2 per cent.

Lower segment operation

Operative results.—L. G. Higgins presents evidence that Caesarean section involves less risk to both mother and child than does difficult vaginal delivery. Of 157 elective operations, twenty were performed for placenta praevia, twelve for severe toxæmia, twenty-one for breech presentation and eighty-eight for disproportion; sixteen were repeated Caesarean sections. In the series here considered the operation was performed before or within six hours of the onset of labour. In many of the patients the lower uterine segment was imperfectly developed and a vertical 'low classic' incision was made; this incision divides only about one inch of active muscle and has been found to heal well without forming adhesions. The maternal mortality was nil, the foetal mortality 5 per cent. One infant died after twenty-four hours, another was premature, a third was anencephalic. Four cases (2.5 per cent) of notifiable pyrexia occurred, the causes being pleurisy and bronchitis (one case), pyelitis (two cases) and uterine sepsis (one case). Of sixty-three operations performed late in labour the maternal mortality was nil, the foetal mortality 4.7 per cent. Notifiable pyrexia occurred in eight cases (13 per cent), resulting from chest conditions in three cases, and from genital infections in five cases. In all these cases labour had been in progress for more than six hours; the lower uterine segment was well developed and a transverse retroperitoneal incision could be and was employed. Some of the most serious risks to the mother from Caesarean section can be overcome by the use of a low incision; the likelihood of subsequent rupture of the uterus and of post-operative obstruction is much reduced. The danger entailed by lower segment elective Caesarean section in a healthy woman should probably not exceed that associated with simple laparotomy. Both the maternal and the foetal risk are increased when operation is performed after prolonged labour. But even in late cases, for example 'failed forceps' cases, Caesarean section is often the safest way of completing delivery. The results of forceps delivery at two large hospitals showed an average maternal mortality rate in elective cases of 1 and in emergency cases of 3 per cent. The foetal death rate in elective cases was 6.75 per cent.

Higgins, L. G. (1943) *Brit. med. J.*, **1**, 212.

Manahan, C. P., Connally, H. F., Jun., and Eastman, N. J. (1942) *Amer. J. Obstet. Gynec.*, **44**, 999.

Tamis, A. B., and Clahr, J. (1943) *Amer. J. Obstet. Gynec.*, **45**, 39.

LABOUR: ANAESTHESIA AND ANALGESIA

See also B. E. M.P., Vol. VII, p. 573; and Cumulative Supplement, Key Nos. 895 and 896

Anaesthesia and analgesia

Methods of administration

Continuous caudal anaesthesia.—W. B. Edwards and R. A. Hingson have used continuous caudal anaesthesia for obstetrical delivery in thirty-three cases, and record their experiences. When given by fractional dosage into the sacral canal, the anaesthetic can be continued without risk for as long as may be necessary; in the present group the average period was about five and a half hours, and the longest period was thirteen hours. The technique which was used is as follows. As soon as the labour pains are well established the patient is placed in the knee-elbow or knee-chest position. The sacral hiatus is located by feeling its inverted V-shaped upper edge at a point 1½ to 2 inches above the tip of the coccyx. After a skin wheal has been raised with the anaesthetic solution a Lemmon malleable silver spinal needle, 16-gauge, is inserted into the sacral canal until the anterior wall is encountered, the amount of penetration being from 5 to 7 centimetres. The needle is then attached to the Lemmon continuous spinal anaesthetic apparatus (incorporating a reservoir and continuous-flow syringe) and 30 cubic centimetres of a solution of 1.5 per cent metycaine in saline is injected at a steady rate during a period of one minute. The needle is secured by strapping, the patient is carefully placed in the lithotomy position, and the vulva and perineum are prepared for delivery. Further doses of anaesthetic solution are given when they are necessary; most patients require an additional 20 cubic centimetres every thirty or forty minutes. Uterine contractions continue satisfactorily, in fact the authors believe that labour was accelerated in all their patients who were anaesthetized as described. Episiotomy and outlet forceps delivery were used in most of the

primiparae. No complications attributable to the anaesthetic were encountered. Three patients vomited once during labour. Resuscitation of the infant was not necessary in any of the cases; one baby was still-born, death having occurred several days before delivery.

The safety of continuous caudal anaesthesia in obstetrics is questioned by N. Block and S. Rochberg after using it in thirty-nine cases. They feel that despite its advantages caudal anaesthesia has certain dangers, notably the risk of introducing the needle inadvertently into the theca, which render it unsuitable for routine use. One patient in the present series suddenly collapsed after five minutes of the procaine drip, ceased breathing and remained unconscious and dependent upon artificial respiration for one hour and a half. This happened despite the fact that before the drip was started suction had been, as always, applied to the needle and no cerebrospinal fluid had been withdrawn. The only symptoms noted in other cases were nausea, vomiting, dizziness, drowsiness and, once, diplopia; they probably resulted from absorption of procaine into the blood stream. The level of anaesthesia was very satisfactory. In thirty-five cases no other anaesthetic was needed. Forceps were applied and episiotomy and repair performed without pain. Bleeding was estimated to be far less than with inhalation anaesthesia. Labour was shortened and cervical dystocia abolished. The patients did not become exhausted and were capable of full cooperation. The absence of anaesthetic effects on the baby is advantageous.

The advantages of continuous caudal analgesia in obstetrics are urged by R. A. Hingson and W. B. Edwards. The aim is to abolish pain and discomfort without interfering with the movements of the legs and the contractions of the uterus. The authors, who have conducted 600 labours without any other anaesthesia, find that provided the level of skin analgesia is kept below the level of the umbilicus, interference with motor function does not result. The dosage was calculated by injecting methylene blue solution through the sacral hiatus in the cadaver. An injection of 30 cubic centimetres was found in sixty bodies to cause staining as high as the tenth dorsal segment and never higher than the sixth, that is not as high as the site of origin of the motor nerve supply to the upper uterine segment. Analgesia is started as soon as the patient begins to feel distressed. The best results are obtained when regular pains are occurring at intervals of five minutes or less. Danger of trauma to mother and child is minimized by the resultant relaxation of the parts. The drug recommended is metycaïne, 1.5 per cent solution in isotonic saline. The skin and ligaments are first infiltrated and a special malleable needle is then inserted through the sacral hiatus into the sacral canal for about two inches, the point lying always below the level of the second sacral spine. Aspiration is performed to exclude an accidental puncture of the dura mater; if this should happen, as shown by withdrawal of cerebrospinal fluid, caudal analgesia must be abandoned owing to the risk of the drug entering the theca in bulk. The authors take the extra precaution of injecting 8 cubic centimetres of the solution and waiting for ten minutes for any signs of spinal anaesthesia to develop. Further doses are injected at intervals as required. T. G. Gready, Jun. and H. C. Hesseltine have used the method in twenty cases with three failures; one patient developed typical shock, and in three cases the results were 'not ideal'. The longest period for which the drug was administered was eight hours. Practically all patients showed a fall of blood pressure, in two cases a rise above the previous maximum being noted as the analgesia diminished. In a Leading Article commenting on the authors' reports the need for special training in the use of caudal analgesia is stressed; the method should be employed only when hospital conditions and skilled obstetricians are available.

Block, N., and Rochberg, S. (1943) *Amer. J. Obstet. Gynec.*, **45**, 645.

Edwards, W. B., and Hingson, R. A. (1942) *Amer. J. Surg. N.S.*, **57**, 459.

Gready, T. G., Jun., and Hesseltine, H. C. (1943) *J. Amer. med. Ass.*, **121**, 229.

Hingson, R. A., and Edwards, W. B. (1943) *J. Amer. med. Ass.*, **121**, 225.

Leading Article (1943) *J. Amer. med. Ass.*, **121**, 260.

LARYNX DISEASES

See also B.E.M.P., Vol. VII, p. 612; and Cumulative Supplement, Key Nos. 918-927.

Acute laryngitis

Treatment

Surgical treatment of acute obstructive laryngitis—Acute obstructive non-diphtheritic laryngitis requiring intubation or tracheotomy is a rare condition, but the fact that the mortality rate is from 50 to 100 per cent makes it an important one. A. H. Neffson reviews 126 cases of patients treated surgically during the last ten years. The organism responsible was in most cases either a haemolytic streptococcus or *Staphylococcus aureus*; the number of cases due to the latter organism has increased remarkably during the last three years. The proportion requiring tracheotomy varied in different years from 4.3 to 19.4 per cent. The death rate averaged 35 per cent, varying in different years in inverse ratio to the number of tracheotomies done; it was lower in patients who had been intubated previously, and was highest in patients under the age of one year. Sulphonamide treatment made no apparent difference to the tracheotomy rate or to the death rate. Intubation is preferred to tracheotomy in all cases in which expert help is always immediately available and when supraglottic obstruction is not present. It must be combined with aspiration, otherwise the tube may become blocked with discharge. Laryngeal ulceration sometimes develops afterwards; this

occurred in 6 per cent of the present series. The death rate was highest (60 per cent) in cases in which intubation failed because of repeated blocking of the tube and tracheotomy was required; the mortality was second highest (30 per cent) in cases so severe that immediate tracheotomy was performed. The author stresses the importance of after-care, especially nasal feeding of intubated patients. Of 153 patients who survived, fifty-one were seen from one to ten years later; twenty-six had had both intubation and tracheotomy, and in two the voice remained hoarse. No change in voice was observed in any patient who had had either intubation only or tracheotomy only. Eleven gave a history of repeated attacks of mild croup.

Paralysis of the larynx

Types of paralysis

Functional aphonia.—The problem of functional aphonia is, as L. H. Clerf and F. J. Brace-land remark, probably as old as man; ancient literature contains many examples of people 'stricken dumb'. The mechanism underlying the functional aphonias will necessarily vary in different cases, but in general it may be said that this hysterical conversion symptom originates in a conflict between the sense of duty combined with the desire for human respect and the impulse to escape from a difficult situation. In the hysterical personality the reaction is complete; the patient loses his voice entirely and his problem is solved, albeit temporarily and pathologically. In the neurasthenic patient the reaction is only partial; he manifests merely hoarseness and often complains of other symptoms as well. The hysterical subject always appears less conscious of his emotional problem than does the neurasthenic. In every case of loss of voice organic disease must first of all be ruled out by full examination, including laryngoscopy which shows, as the only abnormality, failure to maintain adduction of the vocal cords during phonation. When laryngoscopy has been carried out the next step is to discover the difficulty which the aphonia is enabling the patient to evade. The transition of emotional disturbance to physical symptoms is made unconsciously in a personality which is loosely integrated; the question of deliberate malingering does not arise. In many cases aetiological factors are readily discernible and the voice can be restored by simple explanation and suggestion, but sometimes the problem is more complex and the aid of the psychiatrist is required to deal more radically with it. The laryngologist may be tempted to treat any abnormalities demonstrated by his examination in adjacent structures; this is perfectly justifiable if he remembers that, for instance, correction of deviation of the nasal septum will not cure a neurosis. Any form of local treatment may fix the neurosis and cause the patient to concentrate his attention on the part being treated. The authors warn the laryngologist not to become angry with neurasthenic patients, nor to dismiss them with disdain because organic disease of the larynx is absent. He should not delve too deeply into the patient's psychological difficulties; only the more superficial types of psychotherapy are available to him and these, although they may suffice to remove the symptom, cannot cure underlying disorders of personality. Most sufferers from functional aphonia are susceptible to hypnosis, and the authors suggest that the procedure can suitably be carried out by the laryngologist.

Tumours of the larynx

Malignant

Treatment by teloradium.—M. Lederman and W. A. Mill report on thirty-five patients with intrinsic cancer of the larynx who were subjected to teloradium therapy. Nine of the patients had recurrent growths after some other form of treatment and were treated by means of a one-gramme unit. The remainder had not any previous treatment; nine of them were treated by a one-gramme, and seventeen by a five-gramme, unit. The chief advantages of the latter dosage are that each treatment is shorter, penetration is greater and greater accuracy of technique is attainable. All but one of the patients were male; their ages ranged from twenty-five to seventy-nine years, the average being 57.5 years. Clinical evidence of metastasis in the cervical glands was present in two cases. Of the twenty-six primary cases, five were not histologically verified. Biopsy is not insisted upon in the following cases. (1) When severe stridor is present, associated with oedema or with infiltration of the larynx; in many such cases tracheotomy can be avoided by prompt radiotherapeutic treatment, and any surgical interference may render tracheotomy necessary and thereby reduce the chances of cure. (2) In the rare cases in which direct laryngoscopy would necessitate the extraction of sound teeth. Of the authors' twenty-six cases, four were technically suitable for laryngo-fissure or fenestration; the disease disappeared in all after treatment. Ten of the remainder were suitable for laryngectomy; in seven the disease disappeared; the others could not subsequently be traced. Three cases were technically inoperable. One patient is alive and well after eight and a half years. Fifteen of the patients have been observed for at least five years and seven have remained well. Of the nine recurrent cases four were inoperable, but a moderate degree of relief was given. The other five patients were technically suitable for laryngectomy but in only one case would the general condition have justified it; the patient concerned remained well for a year after treatment and was then lost sight of. All the others died of broncho-pneumonia during treatment. The dosage necessary cannot be stated in general terms; in some cases a dose of 5,500 r has sufficed to sterilize the growth, in others a dose of 10,000 r has failed to do so. The dose aimed at is 5,000–7,000 r spread over a period of from four to six weeks, but each case must be judged on its merits and daily examination is essential. Complications which may develop are oedema

of the larynx (sometimes necessitating tracheotomy), necrosis of the larynx and laryngeal stenosis.

Clerf, L. H., and Braceland, F. J. (1942) *Ann. Otol., etc., St. Louis*, **51**, 905.

Lederman, M., and Mill, W. A. (1942) *J. Laryng.*, **57**, 471.

Neffson, A. H. (1942) *Arch. Otolaryng., Chicago*, **36**, 773.

LEAD POISONING

See also B.E.M.P., Vol. VII, p. 658; and Cumulative Supplement, Key No. 931.

Treatment

Sodium citrate solution

S. S. Kety and T. V. Letonoff report fifteen cases in adults of industrial lead poisoning treated by giving sodium citrate. In dilute solution this drug has been shown to exert a powerful solvent effect on the highly insoluble tertiary lead phosphate. The dose administered was 4 or 5 grammes (60–75 grains) of citrate dissolved in 1 fluid ounce of water three or four times a day. Four patients with severe colic also received 50 cubic centimetres of 2.5 per cent solution intravenously on admission, with immediate relief. In nine cases an interval was allowed to elapse before citrate therapy was started. During this control interval no consistent change was observed in the lead concentration of the blood; as soon as citrate was started a fall began. In eleven patients this fall was continuous; in four the initial drop was succeeded by a rise and this again by a further fall. Colic disappeared within twenty-four hours. Constipation did not improve. In six cases basophilic stippling was much reduced by the end of treatment. Of ten patients whose haemoglobin was determined, this rose slightly in three and considerably in three; four showed a slight decrease. Ill effects attributable to the treatment were not observed.

Kety, S. S., and Letonoff, T. V. (1943) *Amer. J. med. Sci.*, **205**, 406

LEISHMANIASIS, CUTANEOUS

See also B.L.M.P., Vol. VII, p. 664; and Cumulative Supplement, Key Nos. 932–934

Oriental sore

Treatment

Antimony injections, sulphonamides, curettage and irradiation.—H. Avery reviews the recent literature relating to the treatment of oriental sore, this form of leishmaniasis is a disease of dry areas and is rarely found in the moist localities where kala-azar is endemic. One attack usually confers immunity. The lesion is a specific granuloma which breaks down into an ulcer; it is usually multiple and occurs mainly on exposed parts of the body. No specific treatment is known, but in most cases the conditions respond to intravenous injections of tartar emetic or other antimony compound combined with some form of local treatment. When the sores are few in number local injections of 2 per cent berberine sulphate into the indurated area surrounding the lesion have given excellent results. Sulphonamides applied locally in ointment or powder form have also been used with success. The local application of phosphorus oil (B.P.) and of fuchsine paint has been recommended. When severe secondary infection is present good results may be obtained by the use of adhesive strapping after curettage of the ulcer; pure carbolic acid or tannic acid may be applied after curetting. Daily applications of carbon dioxide snow have been used successfully. Diathermy has proved unsuccessful. In some intractable cases the lesions have responded to X-ray or Grenz ray irradiation. So far as prevention is concerned, vaccines have given encouraging results.

Avery, H. (1942) *J. trop. Med. (Hvg.)*, **45**, 121.

LEPROSY

See also B.E.M.P., Vol. VII, p. 682; and Cumulative Supplement, Key No. 935

Diagnosis and differential diagnosis

Lepromin test

Three main pathological types.—Speaking on leprosy at the Annual Session of the American Medical Association, V. Pardo-Castello and F. R. Tiant adopted the modern classification into three main pathological types—lepromatous, tuberculoid and non-specific; mixed types exist. (1) The histological features of the lepromatous lesion are those of an infiltrating granuloma with little or no defensive reaction. Very large numbers of bacilli are found in the lesions. Hence these cases are dangerous and the patients have to be isolated. The lepromin test is negative, indicating entire absence of defence. The prognosis is bad. (2) The tuberculoid type shows three different lesions, the miliary, the sarcoidal and a necrotic variety for which the name 'lazarine' has been suggested. The lepromin test is strongly positive. Bacilli are rare in the lesions except in the lazarine type, in which they are abundant in the necrotic areas. The prognosis is good and the danger to others is not great. (3) The non-specific forms of leprosy are really transitional types showing various lesions in which bacilli are rare. The lepromin test indicates which patients are likely to develop lepromatous lesions and which cases to remain non-specific or to become tuberculoid. The histamine test is a useful diagnostic aid in doubtful cases; leprosy skin fails to show the normal erythematous response.

Pardo-Castello, V., and Tiant, F. R. (1943) *J. Amer. med. Ass.*, **121**, 1264.

LEUKAEMIA

See also B.E.M.P., Vol. VIII, p. 1; and Cumulative Supplement, Key Nos. 940-955.

The leukaemias: all types*Morbid anatomy*

Splenomegaly.—E. B. Krumbhaar and A. Stengel have investigated the splenic changes occurring in leukaemia in a series of 209 cases coming to necropsy, and comprising acute lymphatic leukaemia, fifty-one cases; chronic lymphatic leukaemia, forty-eight cases; acute myelogenous leukaemia, forty-four cases; chronic myelogenous leukaemia, forty-seven cases; monocytic leukaemia, seven cases; unclassified, twelve cases. In general, the largest spleens are found in the chronic forms, especially the myelogenous, and in patients who continue to show considerable leucocytosis until death. In about half of the chronic cases the capsule was thickened or adhesions were present. In the lymphatic type the Malpighian follicles were found to be increased in the earlier stages but to disappear as the pulp was invaded by the leukaemic cells, when the histological picture becomes indistinguishable from that of lymphosarcoma. The use of the term leukosarcoma to cover both diseases emphasizes their essential similarity. Fibrosis was found to be most frequent in the lymphatic forms.

Myelocytic leukaemia*Chloroma*

Morbid anatomy.—P. H. Hartz and A. van der Sar record a case of chloroma or chloroleukaemia in a man, aged forty-one years, which was remarkable for the invasive character of its leukaemic cells, and they discuss the nature of the disease, especially with reference to the neoplastic factors. The patient came under observation first with a slowly growing tumour over the sternum; since the Wassermann and Kahn reactions were strongly positive, the tumour was regarded as a gumma. Antisyphilitic treatment was given for a month and the patient then felt so well that he gave up attendance at the hospital until he was subsequently admitted in a desperate state with anaemia and numerous haemorrhages; he died shortly afterwards. The necropsy, which was performed twenty minutes after death, showed a tumour, the size of a man's fist, which was adherent to the skin, sternum and pectoral and intercostal muscles. It was firm, necrotic in the centre but green in colour, as was the marrow of the sternum and of some of the ribs. A similar large green tumour was present in the upper mediastinum, another green tumour measuring 1–3 centimetres was seen in the body of the pancreas, and a similar one was present in the cortex of the left kidney. Microscopically the leukaemic cells were twice or three times the size of an erythrocyte, and the protoplasm was basophilic, the cells were undifferentiated myelogenous elements which had invaded the pectoral and intercostal muscle fibres, blood vessels, lymphatic structures and other tissues in the same manner as do tumours which are generally recognized as being malignant. Emphasis is laid on the malignancy of chloroma and leukaemia. In 1937 E. V. Kandel collected 175 undoubted cases of chloroma, and since then fifteen more cases have been added by Hartz and van der Sar.

Lymphocytic leukaemia*Chronic lymphocytic leukaemia*

Aleukaemic lymphatic leukaemia, or lymphosarcoma.—Under the above title J. W. Auld reports the case of a man, aged forty-one who, two and a half years previously in a motor car accident sustained injury to the scalp; soon after a growth appeared in the damaged area. Within a short time numerous small pinkish tumours were noticed on the forehead and sides of the face and three months before the patient came under observation the left parotid gland became enlarged, tender and very painful. The lymphatic glands and the skin of the head and neck were infiltrated with growth, much of it being telangiectatic. The liver was not enlarged and the spleen was not palpable. After biopsy the first and largest nodule on the scalp was reported to be a form of lymphoblastoma, either aleukaemia or lymphosarcoma. In the group of lymphoblastomas Auld includes several diseases of lymphatic origin, lymphatic leukaemia, Hodgkin's disease, mycosis fungoides and perhaps generalized non-pigmented sarcomatosis cutis. The prognosis in lymphoblastoma is bad, and there is a danger of fatal toxæmia if too large an area is irradiated at one sitting.

Monocytic leukaemia*Chronic monocytic leukaemia*

Aetiology and clinical course.—T. S. Evans reviews in detail the subject of monocytic leukaemia. The monocyte, of which the status has long been precarious, is now accepted by the majority of haematologists as being a distinct type differing from both the myelocytic and lymphatic strains of leucocytes. Its seat of origin is probably the reticulo-endothelial system. Monocytic leukaemia, of which the author has been able to collect 197 cases from the literature, is said to constitute about 2 per cent of all cases of leukaemia. Cases have been recorded in patients of all ages from under one up to eighty-one years, and about twice as often in males as in females. Heredity is not apparently a causal factor. The disease has been observed in white, yellow and black races and in widely separated parts of the world. Evidence has not been obtained that the disease is of infective origin. Some authorities believe that a close relation exists between chronic aleukaemic monocytic leukaemia and Hodgkin's disease. The acute form has been likened to a new growth. The pathological lesions of monocytic

leukaemia consist of hyperplasia of the reticulo-endothelial tissues, haemorrhage and ulceration. Any organ in the body may be invaded by monocytes. The blood contains the cells in numbers varying widely from one case to another and also in the individual patient from day to day. An aleukaemic type occurs. Monocytes are large round or oval cells with abundant cytoplasm which stains in such a way as to resemble ground glass, and contains a group of azurophil granules. The nucleus is round, oval or indented. The mature cells are easily recognized but immature forms may give rise to difficulties in diagnosis, and supravital staining methods may be required for their recognition. Clinically the cases run an acute, subacute or chronic course; the fatal ending is preceded by an illness lasting from days to years. In the acute cases mouth lesions are prominent, haemorrhages into the skin are common and fever occurs. In the chronic cases skin lesions are often present. Treatment is not of any avail in the acute cases, in chronic cases benefit has been reported from X-ray therapy.

Auld, J. W. (1942) *Canad. med. Ass. J.*, **47**, 563.

Evans, T. S. (1942) *Medicine, Baltimore*, **21**, 421.

Hartz, P. H., and Sar, A. van der (1942) *Amer. J. Path.*, **18**, 715.

Kandel, E. V. (1937) *Arch. intern. Med.*, **59**, 691.

Krumbhaar, E. B., and Stengel, A. (1942) *Arch. Path.*, **34**, 117.

LICHEN

See also B.E.M.P., Vol. VIII, p. 41; and Cumulative Supplement, Key Nos. 956-960.

Lichen planus

Aetiology

Endocrine factors.—Mary S. Smith describes a series of cases, all in women, of chronic lichen planus of the palms and soles. Nearly all the patients were over fifty years of age, only three being under forty. Cases were counted only if the diagnosis of lichen planus simplex was confirmed by the presence of lesions elsewhere in the body, as well as on the hands or feet. The majority of the patients gave a history of nervous strain. A history of allergy, alopecia, articular rheumatism or psoriasis was obtained in one-third of the patients. Of twenty-three patients who were tested, eleven showed abnormally low sugar tolerance curves, which have been found also in many cases of allergy. A low curve was observed more often in grey-eyed than in brown-eyed patients, the ratio being 14·9. All the nine brown-eyed patients had glycosuria. It is suggested that lichen planus may be due to exhaustion of the adrenal or other endocrine glands, resulting from repeated stimulation such as might be brought about by worry or emotional strain, or by some antigen. The three chief points in the differential diagnosis from other palmar lesions are the intense itching and the fact that this precedes the appearance of the lesions, the dry appearance of the latter and the slight underlying redness.

Smith, Mary S. (1942) *Brit. J. Derm.*, **54**, 255.

LIVER DISEASES: LIVER FUNCTION TESTS

See also B.E.M.P., Vol. VIII, p. 81; and Cumulative Supplement, Key No. 967.

Scope and significance

Liver function tests and old age

Proof of dysfunction in apparently normal persons.—H. A. Rafsky and B. Newman have studied the response to liver function tests of a group of fifty people (twenty-three male) over sixty years of age. All were free from clinical evidence of disease, including hypertension. The tests were as follows. (1) Hanger's cephalin-cholesterol flocculation test. The reagent was prepared according to Hanger's original directions but was 'ripened' for six weeks. One cubic centimetre of reagent was mixed in a centrifuge tube with 0·2 cubic centimetre of serum and 4 cubic centimetres of normal saline. Sera from individuals with diffuse liver damage cause flocculation; the latter occurred in 32 per cent of the cases in question. (2) The cholesterol partition test. The findings of this test are considered normal if the total serum cholesterol does not exceed 200 milligrams per cent with a maximum free cholesterol value of 40 per cent. The normal limit for total cholesterol was exceeded in 66 per cent of the cases, and the normal limit for free cholesterol in 44 per cent. (3) The bromsulphalein test was performed by administering intravenously a dose of dye equivalent to 5 milligrams per kilogram of body weight. Samples of blood were taken immediately before five minutes after and thirty minutes after; the amount of dye in the serum was estimated colorimetrically. In 26 per cent of the patients the normal limit of 5 per cent in the thirty-minute sample was exceeded. (4) The hippuric acid test. This is performed by oral administration of 6 grammes, or intravenous administration of 2 grammes, of sodium benzoate. The amount of hippuric acid excreted in four hours was estimated and showed retention after oral administration in 12 per cent and after intravenous administration in 24 per cent of cases. These investigations show that liver function tests may yield evidence of dysfunction in a considerable proportion of apparently healthy subjects over sixty years of age.

Sensitivity and reliability

Review of recent findings.—In a paper read at the annual session of the American Medical Association, J. G. Matcer, J. I. Baltz, D. F. Marion and J. M. MacMillan compare the various

liver function tests from the point of view of sensitivity and reliability. These tests should be regarded only as aids to diagnosis and prognosis, indicating merely the functional state of the liver cells and not offering any clue to the cause of impairment. An urgent need exists for further study to define more accurately the limits of normal variation. In cases of functional impairment it is noteworthy that there is not any constant correlation observed between the results of the different tests. The divergence is best explained by the hypothesis that the various functions of the liver are not affected equally by disease. It is a wise precaution to carry out several tests in any suspected case. The tests studied by the authors comprised Hanger's cephalin-cholesterol flocculation test, Quick's intravenous hippuric acid test, a modification of Macdonald's serial bromsulphalein test and Gray's colloidal gold test in relation to one another and to the two older procedures, namely the oral hippuric acid test and the original bromsulphalein test of Rosenthal. Control studies were made of forty normal young adults and normal standards for each test were thus determined. It was found that Hanger's test is reliable only if unripened cephalin is used and if 1+ results are regarded as within normal limits. With Quick's test a urinary output of under 0.70 gramme of benzoic acid as hippuric acid in the one-hour specimen indicates impairment of function. In Macdonald's test twenty minutes, not thirty minutes, is found to be the normal time for disappearance of the dye from the blood stream. Gray's test was found to be unsuitable for routine use. A study of the relative sensitivity of these four tests showed that all are appreciably more sensitive than the two older tests. An improved serial bromsulphalein test was devised, in which the dosage was 5 milligrams per kilogram. The upper normal limit for complete disappearance of the dye from the blood stream is forty-five minutes. Complete disappearance is a much more reliable index than the estimation of the percentage left at a particular time. This test, Hanger's test, and the intravenous hippuric acid test, are approximately equal in sensitivity. The only objection to the larger doses of dye is that some patients experience a transient reaction.

Tests

The hippuric acid test

Its use in surgical prognosis.—An Annotation in the *British Medical Journal* comments upon the comparative neglect in Great Britain of the hippuric acid test of hepatic function, which is popular in the United States of America. This relative unpopularity may be due to theoretical disadvantages such as the uncertain quantity introduced by variations in the rate of absorption. This can be overcome by giving the sodium benzoate intravenously. Impairment of renal function may result in reduced excretion and is a possibility that must be taken into account. This being allowed for, the test appears to be a sensitive indicator of hepatic disease. As a diagnostic aid its usefulness is limited by the fact that it serves merely to indicate that the liver cells are damaged. It is positive in the majority of cases of infective and toxic hepatitis, hepatic carcinomatosis and cirrhosis, and in a considerable number of cases of obstructive jaundice and cholecystitis. The test does not distinguish between these conditions. It may be useful in revealing latent hepatic damage, for example in thyrotoxicosis, and as an index by which to follow the course of hepatic diseases. Prognostically it may enable the surgeon to pick out the poor surgical risk and to institute suitable pre-operative therapy.

Intravenous dextrorotary sodium lactate

Usefulness in diagnosis.—C. Cohn describes the results obtained from a liver function test depending upon the utilization of dextrorotary sodium lactate injected intravenously. Normal hepatic cells are able to convert this substance into glycogen. The test is performed in the following way. The subject, at rest in bed and having fasted for at least twelve hours, is given an intravenous injection of 75 milligrams per kilogram of body weight of sodium *D*-lactate in a 12 to 14 per cent solution. Samples of blood are taken before and thirty minutes after the injection, and the content of lactic acid is estimated in duplicate. With the dose employed, normally acting hepatic cells are capable of removing practically all the injected lactate from the blood within thirty minutes. The retention of as much as 5 milligrams per 100 cubic centimetres of the total dose after this time is taken as indicating some loss of hepatic function. Of thirty-six patients with jaundice due to acute diffuse parenchymal damage to the liver (catarrhal jaundice or toxic jaundice after the administration of arsphenamine) thirty-four retained 5 milligrams or more of the intravenously injected dose of sodium *D*-lactate. Of twenty-four patients with extrahepatic biliary obstruction, in all of whom the diagnosis was confirmed by operation or necropsy, only four showed abnormal retention of lactate. Two of these four patients had a severe cholangitis with associated hepatic damage and a third showed metastatic lesions and an abscess in the liver. As compared with other tests of hepatic function, including the sodium benzoate test, the galactose tolerance test, the urinary urobilinogen dilution test and the ratio of total to esterified cholesterol, the sodium *D*-lactate test proved the most reliable criterion for distinguishing between jaundice due to diffuse liver damage and that due to extrahepatic biliary obstruction.

Serum cholinesterase determination

Review of results.—A. Schiffrin, L. Tuchman and W. Antopol discuss the diagnostic value of serum cholinesterase determinations in biliary disease. The test is based on the fact that the enzyme, in breaking down acetylcholine, produces acetic acid, and the amount of this can be calculated from the volume of carbon dioxide liberated from a carbonate solution. The present study deals with ninety-eight cases, including seventy-five with jaundice and

twenty-three without jaundice. The cases were grouped as follows. (1) Jaundice due to uncomplicated common duct stone (nineteen cases). No cholesterinase values under 40 were found, and twenty-one out of twenty-five observations were over 50. The highest figure was 120. (2) Jaundice due to growth with hepatic metastases (eight cases). Values ranged from 9 to 58, only one being over 50. (3) Jaundice due to cholangitis with or without stone or neoplasm (seven cases). All but one were under 50. (4) Catarrhal and toxic jaundice (sixteen cases). Values ranged from 28 to 100. Of thirty observations, thirteen were under and seventeen were over 50. (5) Hepatic cirrhosis with jaundice (eight cases) and without jaundice (twenty-three cases). Only two had values of over 50, and those with jaundice were under 40. (6) Eight miscellaneous cases of jaundice. Values ranged from 14 to 55. The conclusions are that values under 40 speak against obstruction if metastases and cholangitis can be excluded; values over 40 are against cirrhosis and those over 50 practically exclude it.

Three recently introduced tests

Speed of liver work—A Leading Article in the *Medical Journal of Australia* reviews some of the more recently introduced biochemical tests of liver function. An estimate of liver function is a useful aid to clinical judgment in cases not only of hepatic disease but of thyrotoxicosis, abdominal neoplasm, various chronic intoxications and certain psychoses. (1) The hippuric acid test is a measure of the conjugating and detoxicating functions of the liver. It consists in the administration of 6 grammes of benzoic acid on an empty stomach and the estimation of the urinary excretion of hippuric acid for four hours immediately afterwards. The amount of hippuric acid thus excreted by a normal person is equivalent to from 2.6 to 3.3 grammes of benzoic acid. In 'surgical' types of jaundice it is found that values of less than 1.5 gramme, implying considerable impairment of liver function, mean a bad prognosis. An intravenous modification of this test is said to be much more sensitive than the original method. The patient passes urine and then receives an intravenous injection of 1.77 gramme of sodium benzoate, equivalent to 1.5 gramme of benzoic acid, dissolved in distilled water. The injection should take about five minutes. An hour later the urine is collected and its hippuric acid content estimated. The normal value is equivalent to between 0.70 and 0.95 gramme of benzoic acid. (2) The serial bromsulphalein test, a modification of the original bromsulphalein test and stated to be far superior to it in accuracy, is carried out as follows. The subject is given an intravenous injection of 5.0 milligrams of the dye per kilogram of body weight. Specimens of blood are examined colorimetrically every five minutes for from ten to thirty-five minutes after the injection, and the rate of removal of the dye from the blood stream is thus determined. (3) The cephalin-cholesterol flocculation test is based on the observation that in many cases of hepatic damage the serum is found to be capable of flocculating a colloidal cephalin-cholesterol suspension whereas serum from a normal person seldom or never does so. This test is recommended as a sensitive and useful routine procedure. The tendency in the newer tests is to allow the liver less time to perform its task. A damaged liver may be capable of performing the same amount of work as a normal one but fails to equal the normal liver in speed.

Vitamin K

Prothrombin response.—J. G. Allen and O. C. Julian claim that the prothrombin response to vitamin K is a reliable guide to the condition of the liver cells, and is therefore a means both of differentiating between intrahepatic and extrahepatic jaundice and of gaining an idea as to the progress of hepatic disease. In both forms of jaundice the blood prothrombin level is reduced. In extrahepatic jaundice, in which the liver cells are comparatively undamaged and the prothrombin deficiency results from inadequate absorption of vitamin K, the prothrombin level rapidly returns to normal when vitamin K is given, but in intrahepatic disease, when the liver cells are too much damaged to produce prothrombin, the response is absent or delayed. Three series of cases are reported: all the patients received a daily dose either of 8 milligrams of vitamin K and 2.5 grammes of bile salts by mouth, or of 10 milligrams of vitamin K by injection. (1) In twenty-six patients with obstructive jaundice the average prothrombin level was 54.7 per cent of the normal; after twenty-four hours' treatment the prothrombin was normal in every case. (2) In thirty-one patients with advanced hepatic disease the average prothrombin levels were as follows: before treatment 57.6 per cent; after twenty-four hours, 57.8 per cent; after seventy-two hours, 62.3 per cent. In only one patient did the level reach 100 per cent and that was after seventy-two hours. (3) Four patients with cirrhosis of the liver received vitamin K continuously for some weeks. In two, who improved clinically under treatment, the prothrombin slowly returned to normal; in one of the remaining two the prothrombin remained practically unaltered; in the other the level steadily fell, and both finally died.

EDITORIAL COMMENTARY—The Present day Value of Liver Function Tests

The study of liver disease in man by means of tests of the efficiency of one or other of the numerous physiological functions of the liver cells has two main objects in view. Its wider objective is to throw light on the mechanism of disease by defining the chain or the pattern of disturbance it produces in the normal behaviour of the organism. For example, Quick's hippuric acid test and the bromsulphalein tests have demonstrated that there is impairment of liver function in conditions of thyrotoxicosis (S. S. Lichtman, 1941). The relation of this to the general pattern of the metabolic disturbance in thyrotoxicosis is not yet clear. The observa-

tion has no immediately practical application, but is none the less valuable, on the ground that fuller knowledge of disease processes is likely to lead ultimately to their more effective control.

The narrower objective is to assist in the diagnosis of disorders of the liver and thereby to improve the treatment of patients suffering from them. Here a function test might serve in two ways. It might measure the degree of impairment of liver function and so either indicate the presence of disease before clinical signs make it evident or throw light on the prognosis of disease that is clinically obvious. In this direction the large number of function tests that have been developed, including the recent ones of increased sensitivity, are almost uniformly disappointing: thus, in fifty-two cases of slight and moderate degrees of cirrhosis already recognizable clinically, J. G. Mateer, J. I. Baltz, D. F. Marion and R. A. Hollands (1942) obtained only 66 per cent of positive results with the most sensitive of six modern tests (the intravenous hippuric acid test) and much lower percentages with the others. The occurrence of compensatory regeneration of liver cells in this disease would seem to prevent its early detection by tests of this type. On the other hand the authors quoted, using sensitive tests, found evidence of impaired liver function in many cases of cholelithiasis, and they offer the practical suggestion that such patients would withstand operation better, and show a lower mortality, if they were given a period of high carbohydrate feeding before operation. Incidentally this recalls the fact that the functional behaviour of the liver is not uniform but can vary from day to day, and is greatly influenced by the composition of the diet—a condition not sufficiently taken into account in the performance of many function tests. Moreover all observers are agreed that different functions of the liver vary independently, and any attempt to detect or measure impairment must therefore employ several different tests; those on trial at present are mentioned in the preceding abstracts.

More promising is the attempt by means of function tests to distinguish between jaundice due to obstruction of the larger biliary passages and jaundice due to parenchymatous liver disease, a distinction that is often difficult to draw on clinical grounds alone. The galactose tolerance test, preferably in its intravenous form, has had most success in this direction, and its further exploration, when galactose again becomes available, is to be encouraged. Plasma phosphatase estimation is of some help, but there is an overlap between the range of higher values found in obstructive jaundice and that of lower values found in parenchymatous liver disease; J. B. Rennie (1942) in a recent review of tests of hepatic efficiency discounts the phosphatase estimation on the ground that the higher values merely reflect the absence of bile from the intestine. Cohn's new sodium *D*-lactate tolerance test, although described as expensive, is a promising addition to this group and deserves further study.—ROBERT S. AITKEN.

Allen, J. G., and Julian, O. C. (1942) *Arch. Surg., Chicago*, **45**, 691.

Annotation (1943) *Brit. med. J.*, **1**, 546.

Cohn, C. (1942) *Arch. intern. Med.*, **70**, 829.

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Rennie, J. B. (1942) *Glasg. med. J.*, **20**, 125.

Schiffrin, A., Tuchman, L., and Antopol, W. (1942) *Amer. J. digest. Dis.*, **9**, 342.

LIVER DISEASES: HEPATITIS, ACUTE AND SUBACUTE

See also B.E.M.P., Vol. VIII, p. 104; and Cumulative Supplement, Key No. 973.

Clinical picture

Acute hepatitis

Epidemic types.—N. G. Markoff describes epidemic hepatitis as pre-eminently a military disease. Its chief importance lies in the occasional complications and sequelae, including acute atrophy of the liver, hepatic cirrhosis and pulmonary affections; and in the large scale of some of the war-time epidemics, which may carry a high death rate. Cases should be isolated, and quarantine regulations are recommended by some authorities. The clinical course is divisible into three stages: an initial pyrexial stage with catarrh of the upper respiratory passages; a symptom-free interval; recurrence of pyrexia, usually mild, associated with gastro-enteritis, enlargement of the liver and usually, but not always, jaundice. Various atypical forms have been described. Some cases are associated with very severe headache, others with pyrexial relapses or long-continued mild fever. A meningitic form has been observed. Virus pneumonia may occur. Lowered resistance to tuberculosis, with lighting up of quiescent lesions in the lungs is common.

Acute hepatitis: mild forms

Jaundice associated with infections.—J. C. Ford describes an outbreak of infective hepatitis which occurred in Wembley. The 300 cases which occurred formed part of a more widespread epidemic extending over surrounding districts. The clinical features showed a prodromal phase characterized by pruritus, headache, anorexia, epigastric pain and so on. In only eight

cases were coryza present at the onset. After three or four days nausea, vomiting and fever developed. Bile appeared in the urine on the fifth or sixth day and jaundice occurred twenty-four to forty-eight hours afterwards. With the appearance of the jaundice all symptoms usually disappeared. In some cases the urinary output was much reduced at first, returning to normal with the appearance of biliruria. In all but one case the jaundice disappeared by the end of three weeks. Complications were rare, comprising one case of bronchiolitis and one fatal case of acute yellow atrophy of the liver, confirmed by necropsy. The patients were mostly young, 80·3 per cent being under the age of fifteen and 89·4 per cent under the age of twenty-four. The infective agent and the mode of spread could not be ascertained. It is probable that droplet infection was responsible but this cannot be proved.

Ford, J. C. (1943) *Lancet*, 1, 675.

Markoff, N. G. (1943) *Schweiz. med. Wschr.*, 73, 349.

LIVER DISEASES: HEPATITIS, CHRONIC

See also B.E.M.P., Vol. VIII, p. 118; and Cumulative Supplement, Key No. 974.

Morbid anatomy and pathogeny

Liver

Experiments on dogs.—I. L. Chaikoff, K. B. Eichorn, C. L. Connor and C. Entenman report the production of cirrhosis of the liver in normal dogs as the result of a prolonged high-fat dietary. The observations made on the experimental animals were divided into three groups, which, however, pass without very sharp distinctions into each other, namely (1) the earliest changes of fatty infiltration of the liver cells, (2) increased prominence of the intralobular or intercellular connective tissue, as well as those with actual fibroblastic proliferation and diffuse cirrhosis, and (3) nodular, from regeneration of hepatic cells that had been divorced from their normal portal and central relationship by fibrosis. Five of the livers fall into group (1), ten into (2) and two into (3), one of the two patients of group 3 had been on a high-fat diet for forty-two months. The diffuse fibrosis and cirrhosis was of a mild grade extended over a long period and did not show evidence of inflammation or infection.

Chaikoff, I. L., Eichorn, K. B., Connor, C. L., and Entenman, C. (1943) *Amer.*

J. Path., 19, 9.

LIVER DISEASES: TUMOURS

See also B.E.M.P., Vol. VIII, p. 151.

Malignant tumours

Primary tumours

Aetiology of primary carcinoma of the intrahepatic bile-ducts.—S. Sanes and J. D. MacCallum record two cases, in a man, aged sixty-two, and in a woman, aged sixty-one, in which primary carcinoma, arising from the cells of the intrahepatic bile-ducts, was combined with intrahepatic gall-stones. The possibility that primary carcinoma of the intrahepatic bile-ducts might be due to the irritation of biliary calculi in the intrahepatic bile-ducts—on the analogy of primary carcinoma of the gall-bladder being caused by biliary calculi in the gall-bladder—is discussed, and some previously recorded cases of the above sequence of events are quoted. In both of the authors' cases the intrahepatic ducts were dilated, and in the male patient there was also thrombophlebitic suppuration.

Sanes, S., and MacCallum, J. D. (1942) *Amer. J. Path.*, 18, 675.

LUNG DISEASES: TUBERCULOSIS

See also B.E.M.P., Vol. VIII, p. 182; and Cumulative Supplement, Key No. 988.

Aetiology

Incidence

In Canadian Army recruits.—W. P. Warner reports the results of a survey of men who were rejected for the Canadian Army because of pulmonary tuberculosis, or who developed tuberculosis after enlistment, during the first six months of the present war. All volunteers are examined by X-ray before they are attested. All cases of probable or possible tuberculosis are referred for specialist opinion. Those with small healed lesions are accepted. Larger healed lesions are held to carry too high a risk and lead to rejection, as does evidence of an active lesion or a history of pleurisy during the previous five years. Of 400,000 men who were X-rayed, 3,969 (1 per cent) were rejected for one or other such reasons. The number of cases diagnosed as active was 3,603. On clinical examination alone many of the men would have been accepted; in the group of early cases clinical signs were present in only 20 per cent; in the moderately advanced group in 47 per cent and in the advanced group in 86 per cent. Of 293 patients with cavities 136 had previously undergone clinical examination and in forty-eight the diagnosis had been missed. Routine X-ray examination of volunteers was not begun until two months after mobilization, so that some cases of pulmonary tuberculosis reached the ranks of the Army. A mass X-ray survey of the Army has not been undertaken. Nevertheless only 114 subjects developed pulmonary tuberculosis during the six months of the survey. Ninety-six of the men had been examined radiologically on enlistment; eight only had shown lesions which were not regarded as a bar to acceptance, a figure which appears to justify the

policy of admitting men with small healed lesions. In ten cases the disease was present before enlistment. The average period between the onset of symptoms and admission to hospital was 2·7 months; in spite of this short period thirty-six cases were moderately or far advanced.

In occupational groups of young adults.—F. Ridehalgh presents a preliminary account of work undertaken under the terms of the Prophit Bequest upon the incidence of tuberculosis in young adults. Five groups were studied. (1) A control group of apparently healthy London office and factory workers (704 males and 839 females). Very few came from overcrowded homes. A positive Mantoux reaction occurred in 94·9 per cent of the males and 90·5 per cent of the females, a statistically significant difference. Radiologically, healed primary lesions were found in 5·4 per cent of males and 8·6 per cent of females; there were inactive lesions in 0·8 and 0·7 per cent respectively, and active lesions in 0·14 and 0·12 per cent. Subsequent examinations show that in the contact group subjects originally free from disease develop pulmonary tuberculosis at a rate of from 2 to 3 per cent per annum, so that routine annual review should be of great value. (2) Contacts of cases of pulmonary tuberculosis (379 males, 405 females). In this group overcrowding was more common. The Mantoux test was positive in 97 per cent. Radiologically, healed lesions were found in 15·3 per cent of males, and 19·0 per cent of females, inactive lesions in 2·1 and 3·0 per cent and active lesions in 1·8 and 3·8 per cent. (3) Hospital nurses (1,476). The Mantoux test was positive in 88·5 per cent of voluntary hospital and 83·2 per cent of municipal hospital entrants, but the proportion of negative reactors becoming positive after a year in hospital was 78 per cent in municipal hospitals, as compared with 22 per cent of voluntary hospital entrants. Radiologically, healed lesions occurred in 5·9 per cent of voluntary hospital and 7·8 per cent of municipal hospital entrants, inactive lesions in 0·4 per cent (both groups) and active lesions in 0·0 per cent and 0·2 per cent. (4) Medical students (1,106 males, 141 females). The Mantoux test was positive in 88·1 per cent of males under twenty-one, 90·3 per cent of males over twenty-one; and in 83·7 per cent of females. Radiologically, healed lesions were present in 5·1 per cent of males, 7·1 per cent of females, inactive lesions in 0·09 and 0·7 per cent; active lesions were not discovered. (5) Boys in two naval training establishments (918). In the first, a large establishment giving a year's general training, 66 per cent were Mantoux positive; in the second, a smaller establishment giving four years' specialized training, 78·7 per cent were positive. Most of the boys came from rural districts. Radiologically, healed lesions occurred in 4·9 per cent from the first establishment, 4·0 per cent from the second; inactive lesions were found in 0·0 and 0·8 per cent, and active lesions were present in 0·25 and 0·0 per cent respectively.

In the aged.—The danger of the elderly person with undiagnosed pulmonary tuberculosis as a source of infection is stressed by R. E. Miller and Beatrice Henderson who have made an X-ray survey of 3,414 unemployed adults in New York City, as part of the city's organized antituberculosis campaign. The group contained persons of all ages from fifteen years upwards and did not include any known cases of tuberculosis, any known contacts or persons who had had the chest X-rayed within the previous six months. The results of the survey were as follows. Of all the males examined, 10·63 per cent, and of the females, 6·36 per cent, were found to have unsuspected chronic pulmonary tuberculosis; the percentage of cases of significant tuberculosis was 4·55 in males and 1·6 in females. The 100 cases which were clinically significant were all referred to a clinic for further investigation, and twenty-nine were proved to be active; the criterion of activity was either change (progressive or retrogressive) in the X-ray appearances or positive sputum. The incidence of chronic tuberculosis was decidedly higher in persons above the age of forty; in males the percentages were, under forty, 3·26; over forty, 13·31; in females, under forty, 1·64; over forty, 8·56. The authors urge that more attention should be paid to diagnosis in elderly patients with chronic pulmonary complaints which are often dismissed by their doctors as 'chronic bronchitis' or 'asthma'.

Course and prognosis

Chronic

Rehabilitation.—The Altro model garment factory for discharged sanatorium patients is run with the aim of overcoming physical handicaps by means of graduated work. The patients are kept under medical supervision, and an account of this side of the work is given by L. E. Siltzbach. All patients who stayed at Altro beyond the three months' probationary period, in the years 1915 to 1939, were studied during their stay and after they left to take up work outside. Of the total number of 964, 445 fell into the 'pre-collapse' era and 519 into the era of collapse therapy; of the former about 6 per cent only had been treated by artificial pneumothorax, of the latter 52 per cent had received some form of collapse treatment. The average stay at the workshop was 16·8 months. The patients were divided, according to the results of sputum examination, into three main groups, (1) negative on admission and previously; (2) positive on admission; (3) negative on admission, positive at some previous time. The value of collapse is shown by the fact that in the 'pre-collapse' period the percentage of patients in group (2) was 25, in the later period 6; of patients in group (3) it was 38 and 69 respectively. Of the patients who were observed for ten years after discharge from the workshop (92 per cent), the survival rates were as follows: cases of minimal lesions, 87 per cent; moderately advanced cases, 63 per cent. The significance of the sputum findings is indicated by the fact that, of the patients in groups (1) and (3), 84 per cent survived for ten years, whereas

only 54 per cent of group (2) patients were still living. The mortality among discharged patients was about twice that of general population of similar age and sex composition. For minimum cases the death rate was the same as that of the general population, for moderately advanced cases one and one-half times as great, for advanced cases four times as great. The breakdown rate varied similarly according to the stage of the disease; the patients with persistent negative sputum spent from 86 to 93 per cent of their first fifteen years after discharge a 'well years'.

Blood count

In prognosis.—An investigation has been undertaken by W. Stobie, N. J. England and W. F. McMenemy to discover whether or not regular examination of the blood in patients with pulmonary tuberculosis is of any prognostic value. Two groups of sanatorium patients were examined: 243 patients had pulmonary tuberculosis; eighteen, who were under observation were ultimately diagnosed as being non-tuberculous. In each case the blood was collected from a vein at the same time of day and, in most cases, at intervals of twenty-eight days. Each patient was allowed at least forty-eight hours' rest after admission before the first sample was taken. The tuberculous cases were classified according to the Ministry of Health standard: with further subdivisions into (1) uncomplicated effusion, (2) infiltration without cavitation. The initial blood counts showed that, on admission to the sanatorium, the mean total leucocyte count, neutrophil count and single-lobe neutrophil and Bonsoir count were all higher in the tuberculous than in the control group. In the tuberculous group the values rise steadily from the 'effusion' to the T.B. + 3 patients. The averages for the monocyte eosinophil percentages remain almost stationary. The lymphocyte count declines as the neutrophil count rises. But individual variations are so great that the degree of leucocytosis cannot be taken as an index of the extent or activity of tuberculous disease in any individual patient and the blood count cannot therefore be used for prognosis. Several of the patients showed some degree of secondary anaemia. In women the incidence was highest between the ages of fifteen and twenty years, second highest between twenty and twenty-five and third highest between forty and forty-five. It is suggested that anaemia may be an important causal factor in pulmonary tuberculosis at these ages. In men adolescence is not associated with anaemia, but the incidence increases with advancing years to a maximum between the ages of forty-five and sixty years. The erythrocyte sedimentation rate seems to be the most accurate laboratory index of the activity of the disease, although it is frequently fallacious in individual cases.

Treatment

Cure

Ambulatory pneumothorax.—H. I. Spector and H. E. Oppenheimer describe their experience of ambulatory pneumothorax during a period of ten years. In order to economize in the use of beds at a University Sanatorium, a pneumothorax out-patient clinic was opened in 1931. An initial pneumothorax treatment was never given in the clinic because it was considered to be too dangerous and not the best way of starting pneumothorax treatment. The duration of treatment depended on the type of the disease, and varied from three years for patients with unilateral exudative tuberculosis, to at least five years for patients with caseo-pneumonic tuberculosis with or without cavitation. Before the lung was permitted to expand the patient had to be free from symptoms, the sputum negative for at least a year, the Schilling count normal and the physical signs stationary. Re-expansion was effected by increasing the length of the intervals between refills, by decreasing the amounts given at each refill, or by both methods. While the lung was re-expanding a careful watch was kept for evidence of reopening of cavities or of reactivation of the disease. The results obtained in the clinic were found to justify the method of ambulatory pneumothorax treatment, which also served the purpose of training a succession of medical officers in the principles and practice of pneumothorax therapy for cases of tuberculous and non-tuberculous pulmonary disease.

By cadmium sulphide.—B. A. Dormer, F. J. Wiles and J. Friedlander report from South Africa a series of twenty-six cases of pulmonary tuberculosis in which the patients were treated by cadmium sulphide in addition to having routine sanatorium treatment. Six patients were European and the remainder were Indian or Cape Coloured; their ages varied from sixteen to sixty-four years, the average age being thirty-four. Half the cases were moderately advanced, half were far advanced. Fourteen showed cavitation by X-ray examination, but in three of them the cavity was in the early stages and was thin walled. Twelve patients showed infiltration without cavitation. In one case artificial pneumothorax was instituted and four patients underwent phrenicectomy. The total dose of cadmium sulphide varied from 20 cubic centimetres to 144 cubic centimetres of 1 per cent emulsion in olive oil; the average total was 74 cubic centimetres. The total dose was divided into quantities of 1, 2 or 3 cubic centimetres injected once or twice a week. Toxic symptoms were observed in eight cases; one patient had a rash, seven patients had transient albuminuria. In two other cases the general condition and weight declined continuously during, and for some time after the course of injection and it is thought that the cadmium may have had a harmful effect. Both patients began to improve about three months after the cessation of treatment. Four patients died during the period of treatment. Only one patient showed a degree of improvement greater than that which might be expected in any group of sanatorium cases. All the patients had a positive sputum and in no case did it become negative. X-ray appearances either remained the same

or deteriorated and the erythrocyte sedimentation rate decreased at most by 4 millimetres. The treatment was tried in a group of thirty-eight lepers, with similarly negative results.

High-protein diet.—B. P. Sandler and R. Berke describe the effect of a diet which is low in carbohydrate content and high in protein value, in a group of ten patients with advanced pulmonary tuberculosis. The treatment is based on the assumption that carbohydrate exerts a depressant effect on oxygen consumption and thus lowers the patient's power to overcome infection. The diet which was employed consisted of carbohydrate, 114 to 124 grammes; protein, 101 to 129 grammes; fat, 161 to 212 grammes; the total calorie value ranged from 2,309 to 2,920 calories. Three regular meals were given daily, with feeds of a milk and cream mixture given between meals and at bedtime. Most patients felt hungry on such a diet and lost weight at first, and all began by being antagonistic. All ten, however, showed both clinical and subjective improvement after a few weeks. Five patients returned to their homes, two were rendered fit for surgical treatment, and three were still in hospital but were improving when the report was made. The radiological appearances also improved in some cases.

Results of gold treatment.—A paper read by A. Rest to a meeting of the Denver Sanatorium Association reports 110 cases of pulmonary tuberculosis treated with sanocrysin and oleo-sanocrysin. Gold treatment was begun in 1934 and at first sanocrysin given intravenously was used. After a time, however, a number of complications occurred and oleo-sanocrysin was substituted. This is an oily preparation given by intramuscular injection. Absorption is slower and the likelihood of complications is reduced. Gold treatment was reserved for patients not showing any evidence of renal damage. Almost all developed urinary signs of renal damage at an early stage in the treatment; these disappeared when treatment was discontinued. One patient, however, developed fatal acute nephritis. Other complications were common but usually not serious. Dermatitis was the most frequent, stomatitis came next and colitis third. Neuritis occurred in two cases, haemolytic jaundice in one case and pre-retinal haemorrhage in another. A patient during a second course of treatment developed a haemorrhagic diathesis and died. Minor toxic symptoms such as pruritus, nausea and vomiting were also noted. Small doses were given, starting with 0.05 gramme ($\frac{1}{4}$ grain) every five to seven days and working up to 0.20 gramme (3 grains). After each complete course of 5 to 7 grammes an interval of two to three months was allowed to elapse before another course was started. Of the 110 patients, 105 with advanced disease, twenty-six developed some complication necessitating discontinuance of chrysotherapy when less than 2 grammes had been given, and are therefore excluded. Of the remaining eighty-four, fifteen, or 18 per cent, showed distinct improvement and in seven of these patients sputum conversion took place. In all the cases apparently benefited by gold the lesion was predominantly exudative and infiltrating, that is of the type tending to retrogress spontaneously. The author thinks that in pulmonary tuberculosis gold treatment should be looked upon as the last resort.

Treatment of complications and symptoms

Pleural effusions.—F. G. Chandler enters a plea for conservative treatment of benign serous and purulent pleural effusions, including tuberculous empyema, which most commonly occur in the course of artificial pneumothorax treatment. Such effusions are either sterile on culture or contain tubercle bacilli; they may persist for many years without doing harm and may indeed do good by keeping the lung collapsed. Cases are quoted to show that serous effusions, tuberculous empyema and sterile collections of pus may be benign and may be left entirely alone; the results of active treatment in such cases are often disastrous. Unless signs of toxic absorption are present, or fluid accumulation interferes with establishment of an artificial pneumothorax, the author refrains from any interference, and sometimes even adds olive oil to the effusion to prevent absorption, in cases in which permanent compression of the lung or part of the lung is deemed desirable.

Chandler, F. G. (1942) *Brit. J. Tuberc.*, **36**, 103.

Dormer, B. A., Wiles, F. J., and Friedlander, J. (1942) *Amer. Rev. Tuberc.*, **46**, 164.

Miller, R. E., and Henderson, Beatrice (1942) *Amer. Rev. Tuberc.*, **46**, 164.

Rest, A. (1943) *Amer. Rev. Tuberc.*, **47**, 406.

Ridehalgh, F. (1942) *Lancet*, **2**, 463.

Sandler, B. P., and Berke, R. (1942) *Amer. Rev. Tuberc.*, **46**, 238.

Siltzbach, L. E. (1942) *Amer. Rev. Tuberc.*, **46**, 489.

Spector, H. I., and Oppenheimer, H. E. (1942) *Amer. Rev. Tuberc.*, **46**, 67.

Stobie, W., England, N. J., and McMenemy, W. H. (1942) *Amer. Rev. Tuberc.*, **46**, 1.

Warner, W. P. (1942) *Canad. med. Ass. J.*, **47**, 193.

LUNG DISEASES: TUMOURS

See also B.E.M.P., Vol. VIII, p. 224; and Cumulative Supplement, Key Nos. 992-994.

Malignant tumours of lungs and bronchi

Primary

Bronchial carcinoma, with cardiac infiltration.—B. A. Dormer, J. Friedlander and F. J. Wiles describe the case of a woman, aged thirty-two, who was admitted to the King George V Hospital for Tuberculosis, Durban, in January, 1942 with the following history. In January

1939 an attack of pain on the left side of the patient's chest was diagnosed as pleurisy. The pain lasted for a few days only but had since recurred at intervals. A dry cough, most evident when the patient was lying flat, accompanied the pain; since May, 1941 it had been persistent and sputum tinged with blood had been noted. The woman complained of dyspnoea and fatigue, but not of loss of weight. Examination on admission revealed dullness and increased vocal resonance at the base of the left lung with bronchial breath sounds, and whispering pectoriloquy posteriorly. Her temperature ranged from 97° to 101° F. and she had persistent tachycardia. The sputum was negative for tubercle bacilli and was indefinite for malignant cells. A diagnostic left artificial pneumothorax operation was performed, which showed a limited area of collapse at the base. A tentative diagnosis of malignant disease of the left lung was made. Subsequent X-ray examination showed a rapidly extending opaque area in the left lung, with contralateral invasion and cavitation in the right upper lobe. The patient died suddenly during bronchoscopy. Necropsy showed a tumour occupying almost the entire left lung, infiltrating the right lung; it had penetrated into the left pulmonary vein and from there had entered and had almost filled the cavity of the left auricle. The histological structure suggested a bronchial origin. The immediate cause of death appeared to be massive collapse of the right lung caused by pressure of the bronchoscope on the right main bronchus. The case illustrates the problem of early diagnosis in conditions of bronchial carcinoma.

Estimation of incidence.—Madge T. Macklin has examined the evidence relating to cancer of the lung, to determine whether the supposed increase in incidence is real or apparent. The following are her conclusions. The ratio between necropsies in cases of lung cancer and total necropsies at one large hospital over a series of years shows a pronounced increase. Many fallacies are, however, inherent in this method of approach. For example a disease such as cancer of the lung more often comes to necropsy than does a commoner and more easily diagnosed complaint. It might be thought that the ratio between the number of necropsies for lung cancer and the number for cancer in general affords a more truthful picture, but similar objections also apply here. Improved results of treatment in other cancers may have reduced the number of cases which come to necropsy. If, as is possible (owing to the prevalence of breast and uterine cancers), such results affected the number of females selectively, an apparent increase in lung cancer, which is commoner in males, might be seen. Improvement in diagnosis is unlikely to have affected the number of diagnosed cases of cancer in general so much as the number of lung cancer cases. Statistics which are based on numbers of patients admitted to hospital are open to similar objections. The author believes that the apparent increase in lung cancer can be accounted for largely by improved methods of diagnosis and by the fact that the disease is less affected by advances in treatment than are many others, so that relatively more people die from cancer of the lung. Some real increase, however, has probably occurred.

Lead as an aetiological factor.—The possible influence of lead in the production of bronchogenic carcinoma is discussed by C. E. Black, who has seen two cases in which this factor was present. He points out that lead is closely allied to radium and that the toxic effects of the two elements are strikingly similar. Inhalation of radioactive dust is believed to be an important aetiological factor in cancer of the lung; commercial lead is by far the most radioactive of all the common metals. The two patients reported were both men, aged respectively fifty-seven and sixty-four years. The first had worked for thirty-five years as a linotype operator, in which he was constantly exposed to the fumes of molten lead. He had twice suffered from acute lead poisoning. No family history of cancer was elicited. He complained of weakness, fatigue, left foot drop, diplopia, insomnia and anorexia. He had physical signs of chronic plumbism, and of a neoplasm of the right lung. The urine contained 0.15 milligram of lead per litre. At necropsy a few weeks later the growth was found to originate in the main bronchus to the middle and upper lobes of the right lung. The second patient had been a metal polisher in early life and a painter afterwards. He did not give any family history of cancer. He was admitted to hospital a week before his death, suffering from cough, severe dyspnoea and progressive weakness. No signs of lead poisoning were found. Necropsy revealed an advanced bronchogenic carcinoma of the left lung. The growth appeared to originate in the main bronchus. In both patients the lungs showed chronic fibrotic changes pointing to some form of chronic irritation. The author suggests that inhalation of lead dust or lead fumes may play a part in the development of cancer of the lung.

Total pneumonectomy.—J. Johnson describes total pneumonectomy as a reasonably safe method of treatment for bronchogenic carcinoma or extensive suppurative disease, provided that the patient's general condition has not been allowed to deteriorate too far; he deprecates the delay which often occurs before the surgeon sees the patient. Preliminary bronchoscopic aspiration is valuable in suppurative disease, and in carcinoma with obstruction an attempt at bronchoscopic drainage should be made prior to operation. The author gives sulphonomides for at least twenty-four hours beforehand. During the operation aeration must be maintained and the bronchial tree kept free from secretions. Both these desiderata can best be fulfilled if intratracheal anaesthesia is used. An important technical point is closure of the mediastinal pleura, which much reduces the likelihood of a bronchial fistula. Post-operative care to maintain adequate aeration is of vital importance. In the author's series of twenty cases, six of bronchiectasis, one of multiple lung abscesses and thirteen of carcinoma, only one death took place. The low average age (41.75 years) of these patients doubtless contri-

buted to the low mortality. Two of the patients with carcinoma died of metastasis within a year. Sufficient time has not yet elapsed to enable end results to be assessed.

Non-malignant intrathoracic tumours

Clinical picture

Intrathoracic lipoma.—O. Swineford, Jun. and C. J. Harkrader, Jun. put on record the twenty-sixth published case of a wholly intrathoracic lipoma in a man, aged sixty-two, whose chief complaint was asthma. The authors, however, are not convinced that the lipoma, which occupied the base of the right pleural cavity, as shown by the necropsy, was responsible for the asthma.

Treatment

Pneumonectomy

Effects on respiratory function—In a series of twelve patients, A. Cournand and F. B. Berry have studied the effects of pneumonectomy upon respiratory function. The operation was performed in seven cases for carcinoma of bronchus, in two for bronchial obstruction from other causes and in three for chronic suppuration. In ten patients, divided into two age groups of from thirty-two to forty-seven years (six cases), and of from fifty-three to sixty-six years (four cases), measurements were made of the lung volume, maximum breathing capacity and ventilation at rest and during exercise; from the two last figures the 'breathing reserve' was calculated. The mean lung volume was found to be over the figure calculated for that of a pair of normal lungs, owing to increase in the volume of residual air; the increase was greater in the older age group. Maximum breathing capacity was equal to normal in the older group and above normal in the younger group. The values for ventilation at rest and during exercise were normal in the younger group, in the older group ventilation was above normal at rest, and was much above normal during exercise, return to resting values after exercise was delayed and the tendency to dyspnoea was greater. Oxygen intake and carbon dioxide output per minute were normal in the younger group. In the older group oxygen intake was lowered, especially during exercise, and carbon dioxide output was raised, indicating some loss of efficiency in maintaining gaseous exchange; aeration of the arterial blood, however, remained normal. Abnormal cardiovascular sequelae were not observed. Six patients were studied, both before and after pneumonectomy. The results indicated that the changes in pulmonary function largely antedated operation, that is, they were the result not so much of the operation itself as of the disease for which it was performed. In four patients pneumonectomy was supplemented by thoracoplasty, without additional impairment of respiratory function.

Black, C. E. (1943) *Arch. Path.*, **35**, 366.

Cournand, A., and Berry, F. B. (1942) *Ann. Surg.*, **116**, 532.

Dormer, B. A., Friedlander, J., and Wiles, F. J. (1942) *Brit. J. Tuberc.*, **36**, 169.

Johnson, J. (1943) *Surg. Gynec. Obstet.*, **76**, 460.

Macklin, Madge T. (1942) *Ann. intern. Med.*, **17**, 308.

Swineford, O. Jun., and Harkrader, C. J., Jun. (1942) *Ann. intern. Med.*, **17**, 125.

LUNG DISEASES: GENERAL

Treatment

Surgical treatment

Modern surgery in chest diseases.—The scope of modern chest surgery for lesions other than penetrating injuries is sketched by O. S. Tubbs. (1) In acute empyema it is now agreed that rib resection should not be done until the pus has acquired the consistency of thin cream; repeated aspiration or air-tight intercostal drainage is employed until that stage is reached. After rib resection the drainage tube must be retained until skiagraphy shows complete obliteration of the empyema cavity. (2) Chronic non-tuberculous empyema usually results from mismanagement in the acute stage and the patient should be treated by rib resection and drainage at the lowest part of the cavity. Thoracoplasty may be required in obstinate cases. (3) In lung abscess, when it is acute, external drainage by rib resection under local anaesthesia is required in cases in which postural treatment fails, bronchoscopic aspiration may also be employed. Not more than six weeks should be allowed for trial of conservative measures. A chronic lung abscess usually requires lobectomy, a proceeding rendered safer by preliminary external drainage. (4) In bronchiectasis, removal of the affected lobe or lung gives excellent results in a big proportion of cases and has a comparatively low operative risk. The physical capacity after a successful operation approximates to that of a normal person. (5) Bronchial tumours, of which 95 per cent are malignant, are, in the early stages, amenable to radical operation but at a considerable risk. Irradiation may prolong life but rarely if ever cures the patient. The operability rate is low and inoperability cannot always be determined without an exploratory thoracotomy. (6) Crushing injuries require major surgery only if evidence of continued bleeding or of damage to abdominal viscera is present. (7) In heart diseases surgery is confined to drainage for suppurative pericarditis, to removal of thickened pericardium in Pick's disease, to ligation of a patent ductus arteriosus and to cardio-omectomy for angina pectoris; the last operation is still on trial.

Tubbs, O. S. (1943) *Practitioner*, **150**, 82.

LUNG DISEASES: PULMONARY EMBOLISM

Diagnosis*X-ray methods*

Use of diodrast.—A method of determining the situation and extent of pulmonary embolism by the use of diodrast is described by F. Liberson and I. R. Liberson. They point out that the large majority of post-operative pulmonary emboli are of the non-fatal type but differ from the fatal emboli only in the severity of the symptoms. Most surgeons wait to perform an embolectomy until they feel that the patient has no chance of surviving without it, and so they often wait too long. If the surgeon could know beforehand whether the embolus is likely to be fatal, embolectomy might be performed earlier in suitable cases and would have a better chance of success. The authors' technique is as follows. (1) An artificial embolus is first produced in a rabbit by introducing an embolus-producing, non-toxic, opaque material directly into the right ventricle. This was done by means of a large needle filled with the material, which is passed into the ventricle through the chest wall and emptied with a stilette. Lead filings were found to give the best results. (2) Non-opaque emboli of paraffin were subsequently used and diodrast (diodone) employed to locate them. Absence of filling of the pulmonary arteries below the embolus was the significant finding. A special plate-changer was used allowing six exposures to be made in under eight seconds. The method should be applicable to man. If the embolus is blocking a branch so small that absence of filling is not visible to the radiologist it is likely that the patient will recover.

Liberson, F., and Liberson, I. R. (1942) *Amer. J. Roentgenol.*, **48**, 352.

LUPUS ERYTHEMATOSUS

See also B.E.M.P., Vol. VIII, p. 244; and Cumulative Supplement, Key No. 1004.

Bacteriology and morbid anatomy*Associated affection of glands*

R. A. Fox and P. D. Rosahn record three cases with necropsies and at the same time analyse 277 collected cases with special reference to the question of the associated enlargement of the lymphatic glands in lupus erythematosus. At the beginning of this century the tubercle bacillus was regarded as the responsible cause of lupus erythematosus disseminatus. Since then this opinion has undergone correction, and the histological changes have been found by the authors in their three cases, and by others, not to be tuberculous. In the lymphatic glands, of which those in the neck are most often enlarged, the lymphoid cells are to a great extent replaced by large cells with oedema, hyperaemia and areas of necrobiosis which may have been regarded as evidence of tuberculous infection. These features suggest but are not specific for the disease. Of the collected cases females were affected in 228 and males in 49. There were 214, or 84.6 per cent, under the age of forty years. One case was of special interest because of the absence of skin rashes (*lupus sine lupo*).

Fox, R. A., and Rosahn, P. D. (1943) *Amer. J. Path.*, **19**, 73.

LYMPHOPATHIA VENEREUM

See also B.E.M.P., Vol. VIII, p. 287; and Cumulative Supplement, Key No. 1017.

History, pathology, treatment*Review of the disease*

Opening a symposium on lymphogranuloma inguinale at a meeting of the Victorian Branch of the British Medical Association H. F. Bettinger reviewed the historical and pathological aspects of the disease. Descriptions of lymphogranuloma inguinale appear in ancient Greek, Roman and Arabian medical literature. Galen and Celsus were both familiar with it. But up to the middle of the nineteenth century, all forms of bubo, however much they differed clinically, were thought to be due to one 'venereal disease'. At this epoch it began to be recognized that enlarged inguinal glands were not always the result of syphilis. Wallace of Dublin was probably the first to distinguish a type of indolent bubo which ran quite a different course from that of syphilitic bubo. In the field of tropical medicine a 'climatic bubo' was described. Not until 1930, however, did Hellerstrom and Wassén prove that climatic bubo and lymphogranuloma inguinale are both caused by the same virus. The disease has been reported in every European country, America, Asia and Africa, and a few cases have been observed in Australia. Pathologically the initial changes are predominantly epithelial. The lesion is herpetiform in appearance and not so characteristic that a diagnosis can be made with certainty. After the infection reaches the inguinal glands typical changes take place. The cut surface of an excised gland is studded with tiny stellate abscesses. Microscopical examination reveals that these consist mainly of epithelioid cells arranged in groups with central necrosis. Inclusion bodies are seen in some of the cells. The same typical lesions occur in the rectum in cases, most often seen in women, in which this is involved. F. M. McDonald described treatment as unsatisfactory. Rest in bed and the application of heat to the glands and of antiseptics after the abscesses have burst are reasonable procedures. Some authorities advocate excision of the glands in early cases. Vaccine therapy is said to give good results. Pyrexial treatment has proved useful in the author's hands. H. J. Johnson, Jun. discussed the laboratory findings. The virus of lymphogranuloma inguinale is relatively large and is

stained by aniline dyes. It is visible in the cytoplasm of the histiocytes of involved tissue stained by Giemsa's method. It can be grown on the chorio-allantoic membrane of the chick embryo. Infection in man and in animals is followed by development of cutaneous sensitivity to inactivated virus and of humoral antibodies. Frei introduced a diagnostic skin test. The serum globulin is raised.

Bettinger, H. F. (1943) *Med. J. Aust.*, **1**, 23.

Johnson, H. J., Jun. (1943) *Med. J. Aust.*, **1**, 28.

McDonald, F. M. (1943) *Med. J. Aust.*, **1**, 25.

MALARIA

See also B.E.M.P., Vol. VIII, p. 304; and Cumulative Supplement, Key Nos. 1018 and 1019.

Clinical picture

The attack

Benign tertian and malignant subtertian types.—P. H. Manson-Bahr, discussing the subject of malaria in war-time, describes the two types, benign tertian malaria and malignant subtertian malaria. In the former the parasite's reproductive cycle occupies forty-eight hours, and the classical temperature chart of the disease is unmistakable. Rigors occur on alternate days at exactly the same time. The temperature shoots up to a considerable height, sometimes even to 106° F. Sudden fever, especially when it begins in the forenoon or afternoon, is more likely to mean malaria than any other disease. The temperature falls in an equally abrupt way to a sub-normal level at the end of the attack. The response to quinine given intramuscularly may be dramatic but recurrence is not prevented by a single injection. The fever is not always of the classical type which may not become established until the disease has continued for several weeks. Atypical cases are to be expected, especially in primary infections. Subtertian malaria is a totally different disease. Infected erythrocytes tend to agglomerate so that the development of the parasite proceeds mainly in the capillaries of the internal organs, and the clinical picture varies according to the organ chiefly affected. The fever usually has a quotidian periodicity, but may produce almost any kind of temperature chart; a double rise of temperature, or a dicrotic notch, is very suggestive of subtertian malaria. It is often difficult to find the parasite in the peripheral blood. The carrier of malaria, the *Anopheles* mosquito, is characterized by its attitude; it may be said to stand on its head. It has spotted wings and tends to frequent nooks and crannies. Mosquitoes of this sort are best killed at sight. In human beings the parasite has a limited span of life. The tertian malaria parasite disappears within three years; the quartan parasite is the most persistent and may cause relapses after many years.

Treatment

Prophylaxis and cure

Survey of drugs in use.—W. Hughes and F. Murgatroyd consider the problem of drug control of malaria. They point out that despite their efficacy in the acute attack neither quinine nor mepacrine hydrochloride completely overcomes infection; and when used prophylactically they do not prevent the parasites from establishing themselves and often fail to prevent clinical manifestations of the disease. A further difficulty in war-time is the shortage of quinine, but this may be overcome to some extent by the use of cinchona bark from South America. The only synthetic substitute of any value is mepacrine hydrochloride (atebrin). Either drug will cut short the acute attack but it is doubtful whether suppressive treatment is advantageous, since it appears to inhibit the normal immunological response to infection, so that relapses are more apt to occur. Suppressive treatment, however, is essential for European troops operating for limited periods in malarial regions, because naturally acquired immunity cannot come into play to protect them and their fitness must be maintained. Either quinine or mepacrine hydrochloride can be used successfully in this way. The optimum dosage and spacing are still matters of controversy. Careful supervision is necessary to prevent evasion of treatment, failure of absorption and so on. The importance of recognizing atypical clinical cases of malaria is stressed.

Hughes, W., and Murgatroyd, F. (1943) *Lancet*, **1**, 699.

Manson-Bahr, P. H. (1942) *Brit. med. J.*, **2**, 461.

MALINGERING

See also B.E.M.P., Vol. VIII, p. 354; and Cumulative Supplement, Key No. 1020.

Aetiology

Malingering in the Services

Psychopathology and the choice of symptoms.—The malingeringer is defined by R. Good as a psychopath without guilt feeling for his actions. His conscious assumption and exploitation of symptoms is apparently determined by a masochistic and infantile dependent attitude, and is a defence mechanism against intense anxiety. The author has encountered only three cases in civil life; in war-time cases in the Forces appear to be more common; they must not be confused with hysteria. Six cases reported illustrate the conclusion that the process determining choice of symptoms is emotional rather than intellectual; in all cases desire for punishment was dominant, and several patients exhibited infantile craving for mother or

mother substitute. The disposal of malingers in the Forces is determined solely by considerations of morale and efficiency; they must be ruthlessly weeded out.

Good, R. (1942) *Brit. med. J.*, 2, 359.

MATERNAL MORTALITY

See also B.E.M.P., Vol. VIII, p. 394; and Cumulative Supplement, Key No. 1026.

Causes of maternal mortality

Influence of age

Complications in elderly primigravidae.—P. B. Wahrsinger and J. I. Kushner have examined the grounds for believing that labour becomes more difficult in elderly primigravidae. In a series of 111 women aged thirty-five and more, who were pregnant for the first time, they found that the average duration of labour was 18.9 hours. Spontaneous delivery took place in 49 per cent and low forceps were applied in 28 per cent of the cases. In 9 per cent the mid-forceps operation was used, the indications being a persistent occipito-posterior position, inertia and sudden foetal distress. Caesarean section was performed in 11.7 per cent after a test of labour, the indications being disproportion and fibroid tumours, and toxæmia and cervical stenosis for which the operation was elective. The only deaths (three in number) occurred in patients who were delivered by Caesarean section; in one death occurred four hours after the operation had been performed on account of toxæmia, one patient died from broncho-pneumonia and one from paralytic ileus. The foetal mortality was 9 per cent; if macerated foetuses are excluded, it was 4 per cent; this mortality rate was twice as high as in a series of 10,000 younger primigravidae. It appears, therefore, that the risk to the child is considerably increased in elderly primigravidae. The duration of labour does not appear to be increased in such patients.

Wahrsinger, P. B., and Kushner, J. I. (1942) *Amer. J. Obstet. Gynec.*, 44, 505.

MEASLES

See also B.E.M.P., Vol. VIII, p. 412; and Cumulative Supplement, Key No. 1027.

Clinical picture

Clinical types

Haemorrhagic measles—A case of haemorrhagic measles in a boy twelve months of age is described by J. J. Linchan. The illness started four days before the child was admitted to hospital as suffering from measles complicated by broncho-pneumonia. On admission he was collapsed, cyanosed and dyspnoeic, with a respiration rate of 70. The rash, described by the family doctor as typical, had completely disappeared. Abnormal physical signs were not found in the chest, and the diagnosis appeared to be measles of the suffocative type. The child was given 0.5 gramme (8 grains) of sulphapyridine four-hourly for four days, continuous nasal oxygen and plenty of glucose drinks. Shortly after his admission extensive haemorrhages suddenly began to appear into and under the skin of the face and limbs, reaching a maximum in the course of a few hours. The child began to improve, but remained very ill with an irregular intermittent rise of temperature for nine days, after which convalescence set in.

Complications

Measles encephalitis.—A. R. Peale and P. F. Lucchesi report the following unusual case. A coloured female child, aged five years, was admitted to hospital with measles of ten days' duration and with cerebral symptoms. She was stuporous when left alone, irritable when disturbed. On examination Kernig's sign was doubtfully positive, neck rigidity was moderately pronounced and nystagmus was present, increasing when the child was moved. The heart was not enlarged; a coarse systolic murmur was heard at the apex. Patchy consolidation was present in both lungs. The temperature, pulse and respiration were 104° F., 160 and 60 respectively. Soon after admission the temperature dropped to 97° F., and generalized convulsions occurred. Death took place within thirty-six hours of admission. At necropsy the vagina was found to admit the middle finger with ease; discharge was not noted. The heart weighed 130 grammes. Milk spots were present on the epicardial surface in front and behind. The left ventricle was hypertrophied and dilated. The endocardium of the left auricle and ventricle was thickened and opaque, and microscopical examination disclosed deposits of dense collagenous material containing numerous elastic fibres, that is so-called foetal endocarditis was present. Both lungs showed areas of broncho-pneumonia. The medullary part of both adrenal glands contained deposits of calcium. The uterus yielded microscopical evidence of chronic endometritis and a right pyosalpinx was present, containing thick green pus; smears from this pus showed gonococci. The brain showed moderate oedema and congestion, and histological signs of meningo-encephalitis with a predominance of lymphocytes in the inflammatory exudate. Measles encephalitis was regarded as the cause of death.

M. F. Shaffer, G. Rake and H. L. Hodes describe a case of fatal encephalitis complicating measles in which virus was isolated from the brain. The causation of encephalitic signs with or after measles has been much discussed. Although many authorities believe that the neurotropic properties of the measles virus are responsible, others consider that

the manifestations are toxic or allergic in origin or are due to secondary invasion by another pathogenic agent. In the case reported a seven-year-old boy developed typical measles and four days after the appearance of the rash he developed sudden headache, loss of consciousness and convulsions. On admission to hospital the rash, haemorrhagic in places, was still visible. Blood culture and agglutination tests ruled out meningococcal septicaemia and Rocky Mountain spotted fever. The child was treated by sulphadiazine orally and intravenously, digitalis and sedatives, but died without regaining consciousness on the fifth day after admission to hospital and nine days after the appearance of the rash. Necropsy was performed within six hours of death. The brain was removed under aseptic conditions and samples of the cerebral cortex, medulla and pons were taken, pooled, ground with alundum and made up to a 1 in 40 dilution in sterile broth. The mixture was centrifuged and the sediment discarded. Cultures, aerobic and anaerobic, from the supernatant fluid proved sterile except for two colonies of staphylococci which grew on one agar plate. The supernatant fluid was used to inoculate experimental animals of several kinds. Evidence of the presence of herpes virus was not obtained but two monkeys developed a disease indistinguishable from measles. Egg inoculations gave negative results. The authors draw attention to the unusual length of time during which the measles virus must have persisted in the body and to the probability that the virus was the cause of the encephalitis.

Course and prognosis

Assessment of mortality rates

Results of modern therapeutic advances.—The mortality rates from measles are analysed by W. J. Martin in an endeavour to assess the results of new methods of treatment. The number of deaths from measles in successive two-year periods has shown an almost uninterrupted fall since 1922–3. The trend of mortality has probably been influenced by improved standards of nutrition and hygienic conditions and, in London, a larger proportion of patients are treated in hospital, as well as by serum prophylaxis and by special therapeutic measures. Possibly, also, the virulence of the organism may have declined. It is impossible to assess the relative importance of these various factors in bringing about the decline in mortality. Since measles was made notifiable only a few years ago the case mortality rates cannot be compared but, when due allowance is made for the fall in the population at ages 0–15 years, it is found that the childhood mortality from measles is nowadays only about three-quarters of what it was twenty years ago, with a corresponding saving of children's lives. If the deaths are related to the average population aged 0–15 in 1922–5 and this factor is applied to the estimated population at a similar age in 1940–1, the resulting expected deaths for 1940–1 would be 6,593 in excess of those actually recorded.

Treatment

Symptomatic

Results of sulphonamide therapy.—H. S. Banks describes the improved results obtained in measles by the use of the sulphonamide drugs. Small doses may be given prophylactically, and a significant fall in the mortality rate and in the incidence of complications has occurred as a result of sulphonamide administration. Thus in one hospital, the percentage of cases of both otitis media and broncho-pneumonia has fallen from 13 in 1933–4 to about 4 in 1940–1, and the mortality rate has decreased from 6.5 to 0.5 in the same period. The dosage advised for prophylactic purposes is sulphapyridine 1 gramme (15 grains) daily for patients below the age of two years, 2 grammes (30 grains) daily for patients above that age, administration being begun as soon as the diagnosis is made and being continued for five days after the rash appears.

EDITORIAL COMMENTARY—Epidemiology and Treatment of Measles

The epidemic of measles which occurred in 1942–3 was the most extensive and probably the most severe since the last epidemic of 1937–8. It will be noted that the rhythm of the regular biennial periodicity beginning in each odd year, but interrupted by the war and the changes it brought in its train, has not been resumed. Comparative figures of incidence are not available, since measles was not notifiable in England and Wales generally until November 1939, but the death rates per million children under fifteen years for the years, 1937–42, serve as a pointer: 2.6, 4.0, 0.7, 2.1, 2.8. There is general agreement that the current type of measles is mild but an exceptionally high prevalence of bacterial infections, particularly streptococcal, has resulted in a heavy incidence of complications, particularly otitis media and mastoiditis. Some practical points in connexion with measles control have come to light in the last few years.

Although the virus of measles has been successfully grown (Plotz, 1938; Shaffer, Rake and Hodes, 1942; Mayer, 1941) on chick embryo media and transferred to susceptible monkeys as well as to human volunteers, the method is too specialized and costly to find a place, as yet, in the diagnosis of doubtful cases. Apart from Koplik's spots which all too frequently have disappeared by the time the practitioner is called to see the patient, there is nothing pathognomonic in measles. The finding of Turck and plasma cells in the blood serves to differentiate measles from all other exanthemata, with the exception of rubella which resembles it closely, especially in adults.

The onslaught of measles falls most heavily upon the young and debilitated, especially those suffering from respiratory or gastro-intestinal affections and from hypovitaminosis. Some

adults prove highly vulnerable, particularly in pregnancy; but even under the most favourable circumstances measles may be serious or even fatal, and a return to the deadly epidemic of 1915 is always a possibility. Recently J. H. Mulvany (1942) described eight cases of sudden suffocative laryngitis which he ascribed to oedema of the glottis, not—as is the general experience—to laryngeal diphtheria. It is probable that a streptococcal invasion was the cause in most of the cases but in the absence of laryngeal swabs the existence of diphtheria could not be disproved; certainly the absence of membrane formation is not any proof. Only two patients recovered, one after tracheotomy, the other without operative interference.

The hygiene of the mouth, nasal passages and eyes is important in averting serious complications. Stomatitis is prone to be troublesome in debilitated patients who should be treated actively by vitamins, especially A, B and D. The suggestion that riboflavin and nicotinic acid are more specific has not been proved by clinical trial. Potassium chlorate (1 in 40) and sodium perborate (1 in 40) in watery solution are better than the time-honoured borax in glycerin as local applications. Sulphathiazole ointment is useful for cracked lips and impetigo.

Home nursing of uncomplicated cases is preferable to hospital treatment because of possible overcrowding and bad ventilation in hospitals, with the consequent increased risk of cross-infection. For serious complications such as pneumonia, mastoiditis, enteritis and encephalomyelitis the special skill and therapeutic resources of hospitals will always offset the risks incidental to hospital treatment. Panophthalmitis and cancrum oris, formerly common complications, have now virtually disappeared, thanks to improved nutritional and hygienic conditions generally.

Recent methods of preventing infection and cross-infection in hospitals have greatly reduced these risks but they are not applied everywhere either because of shortage of materials and trained staff or because isolation units, being largely constructed of glass, are unfit for occupation on account of air-raids. Such measures as oiling of floors, and to a less extent of fabrics, to allay germ-bearing dust are well known and are employed in some hospitals, but air-conditioning of rooms and purification of atmospheres by aerosols or by ultra-violet irradiation have not found much acceptance, chiefly because of war-time difficulties. The subject has been given the status of an applied science in the United States of America where the newer methods, especially irradiation, have been used extensively in hospitals and schools. Both theoretical and practical problems are fully discussed in a recent volume entitled 'Aerobiology'.

As regards the treatment of complications, all workers are agreed that broncho-pneumonia responds well to the sulphonamides, although not in the dramatic fashion one expects in lobar pneumonia. I. Telegdi (1942), using ultraseptyl (sulphamethylthiazole), reduced the case-fatality from 63·7 to 28·5, a figure which remains high by standards in Great Britain. Dosage was moderate: 1·5 gramme (25 grains) daily for children under three years, from 2 to 2·5 grammes (30 to 37½ grains) at ages four to ten and 3 grammes (45 grains) over ten.

Immune measles serum finds little place in treatment although young subjects with severe attacks are occasionally given one dose, preferably intravenously, at the onset. The Council of Pharmacy and Chemistry of the American Medical Association in a recent report (1943) concluded that even the most potent serums had little place in treatment.

Convalescent serum is the prophylactic of choice particularly when protection is the aim. The occasional occurrence of toxic hepatitis appearing from one to three months or longer after the injection of certain batches emphasizes the need for the greatest care in the selection of donors and harvesting of the serum. The subject has been fully discussed in a Memorandum (1943) by medical officers of the Ministry of Health who were unable to come to a decision whether or not hepatitis is allergic in origin or is the result of the introduction of a contaminating specific virus. On the evidence available the latter explanation is the more probable.

The place of immune globulin (placental extract) in measles prophylaxis has not been finally evaluated, although the Council on Pharmacy and Chemistry (mentioned above) decided that there was little to choose between it and convalescent serum. In my own experience convalescent serum usually confers 100 per cent protection whereas immune globulin has been found to be only slightly superior to adult serum, especially if procured in the same way as placental products. Inoculation reactions, however, are just as prone to occur and the benefits of concentration are more than offset by the unpleasant side-effects. A convenient dosage scheme of convalescent serum is: (1) for protection to children under three years, 5 cubic centimetres, and thereafter age \times 2 up to a total of 20 cubic centimetres given on or before the fifth day after exposure; (2) for attenuation the doses should be given between the sixth and ninth days, or halved and given in the first five days. Adult serum is best reserved for attenuation purposes and should be given in doses twice or thrice those of convalescent serum.

Too frequently supplies of convalescent serum are not available at the beginning of an epidemic when needed most or stocks collected during a previous epidemic have deteriorated, with loss of protective power ranging from 25 to 50 per cent. To obviate such wastage it is now customary to dry the serum by skin-freezing *in vacuo* (R. I. N. Greaves and Muriel E. Adair, 1939). Reconstitution is readily effected.

An attenuating dosage of immune serum after deliberate exposure of the patient is the only practicable procedure for active immunization but it does not appear to have been used on any scale. The experimental work of J. Stokes, Jun., and G. Rake (1940) gives grounds for

the hope that, in the not too distant future, campaigns for measles immunization will be as widespread and profitable as diphtheria immunization programmes are at present.

School closure is now largely replaced by a policy of exclusion of immediate contacts for a week beginning a day or two before the end of the incubation period. Infants' departments are still closed by some school authorities while older contacts are permitted to attend school but are subjected to daily inspection by the school nurse or doctor and excluded on the suspicion of measles appearing. This policy has been recommended for some years by the Medical Officers of Schools Association in their Code of Rules (revised 1940). It is primarily applicable to public and preparatory schools but is also suitable for elementary and secondary schools. Official endorsement of the new policy was incorporated in a Memorandum (1942) on Closure and Exclusion from School issued jointly by the Ministry of Health and the Board of Education in the following terms. 'The principle relating to the closure of schools enunciated in the Memorandum, that it is only in special and quite exceptional circumstances necessary to close a school in the interests of public health, still holds good.'

Two rare conditions call for special notice. Despite the statements of several clinicians with extensive experience of fevers that they had never encountered an instance of haemorrhagic measles, cases purporting to be authentic continue to be reported occasionally. The case reported in the abstracts above appears to be one of severe haemorrhagic staining with bullous impetigo on the nose.

A solution of the obscure problem of the aetiology of measles encephalo-mylitis—the second of the above conditions—and probably of allied invasions of the central nervous system appears to be provided by the researches of Shaffer, Rake and Hodes. They inoculated suspensions of infected brain tissue into chick embryos with negative results, and into two small monkeys with subsequent development of measles and immunity to later inoculations. One of the monkeys had temporary paresis of one arm and leg, making it likely that a neurotropic variant of the measles virus, rather than a special susceptibility in the patient was responsible. It is unlikely that immune measles encephalitis serum would be of value in treatment but it is worth trying since apparent success has been reported in one or two cases. A recent severe case (unpublished) under my care recovered after injections of calcium gluconate.

It is generally assumed that patients with measles cease to be infectious after the fourteenth day from the onset, in the absence of complications. It is now recognized that complications do not have any bearing on the duration of infectivity which some authorities consider to be less than fourteen days, probably twelve days.

Current disinfection of infectious discharges and contaminated articles must be prompt and effective since the disease is highly contagious, especially in the early stages. On the other hand, once infectivity has ceased in the host terminal disinfection may safely be limited to a thorough 'spring-clean' with liberal use of soap and water.—WILLIAM GUNN.

American Association for the Advancement of Science (1942) *Aerobiology*, Washington, p. 289.

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Greaves, R. I. N., and Adair, Muriel E. (1939) *J. Hyg., Camb*, **39**, 413.

Linehan, J. J. (1942) *Brit. med. J.*, **2**, 725.

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Memorandum by Medical Officers of the Ministry of Health (1943) *Lancet*, **1**, 83.

Memorandum on Closure and Exclusion from School (1942) H.M. Stationery Office, p. 2.

Mulvany, J. H. (1942) *Brit. med. J.*, **1**, 638.

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Shaffer, M. F., Rake, G., and Hodes, H. L. (1942) *Amer. J. Dis. Child.*, **64**, 815.

Stokes, J., Jun., and Rake, G. (1940) *Science*, **92**, Supplement (Sept. 20) p. 10.

Telegi, I. (1942) *Klin. Wschr.*, **13**, 300.

MEDIASTINUM DISEASES

See also B.E.M.P., Vol. VIII, p. 438; and Cumulative Supplement, Key No. 1028.

Classification

Mediastinal emphysema

Hamman's disease.—D. S. Munroe and G. A. C. Webb record a case, in a man aged twenty-one, of a condition rarely diagnosed—spontaneous mediastinal emphysema—and describe the clinical features. On 19th May, 1942 the patient came under observation with pain in the precordial region of two days' duration, made worse by exertion; there was also a scraping sensation in the area of the apex of the heart. He gave a history of a similar attack in September,

1941. In the condition now under consideration, improvement followed rest, but two relapses occurred at short intervals, and in a localized area at the apex beat an extremely rough, rasping, crackling, loud to-and-fro murmur with two phases, became audible. This may be caused by exertion, straining, and labour. On experimental grounds it has been thought by C. C. Macklin that there is a group of persons with a liability to leakage of air, as in pneumothorax, and that the air is absorbed in one or two weeks. The condition was described in 1934 and 1937 by L. Hamman, and the most characteristic physical sign—the sound at the apex of the heart—has been called Hamman's sign by Munroe and Webb, who point out that it may easily be missed as it may be present only in the left lateral region. Another positive, if not diagnostic, sign, is the reduction or abolition of the normal area of cardiac dullness; the note may even be hyperresonant. The occurrence of mediastinal emphysema may be due to serious lesions, but the pain may come on during rest or sleep, and when the cause is not obvious, is called spontaneous. The pain may be severe in adults, but the prognosis is good; in infants the prognosis must be guarded, as death may be sudden. Cyanosis may occur, but the other physical signs may be much the same as in adults. The treatment is usually symptomatic only, but aspiration is indicated by increasing dyspnoea and cyanosis and has sometimes had a truly dramatic effect.

R. M. Lintz adds one more case to the twenty-one previously published cases he has collected of spontaneous mediastinal emphysema, described by L. Hamman and even spoken of as Hamman's disease. The patient, a male, aged twenty-two years, was suddenly, while resting quietly, attacked by severe pain in the left side; the latter seemed to be more resonant over the praecordium; anteriorly from the left costal margin to the third rib 'boiler-like' sounds of loud intensity were audible, an hour after the patient's admission to hospital, examination of the chest showed marked diminution of these sounds and two hours later they had disappeared and their place was taken by a few crackles. Improvement rapidly took place afterwards. Radiologically there was on admission a small pneumothorax at the apex of the left lung, but no air was visible in the mediastinum. Hamman, who has done much in making the profession familiar with this syndrome, has concluded that interstitial emphysema of the lung may occur without the least effort when the affected person is quietly standing, sitting or lying down: when air reaches the mediastinum there is pain, often very severe, but without shock; in many cases there is a peculiar and distinctive sound over the heart synchronous with its contractions, and usually during systole only, but sometimes during diastole only. The area of cardiac dullness may be diminished or completely obliterated. Pneumothorax is common.

As a result of war injury.—In the course of a review of war injuries of the chest H. K. Gray writes: 'Closely associated with tension pneumothorax may be the problem of subcutaneous emphysema or mediastinal emphysema or both because the mechanical effect of muscular activity in these circumstances may force air through a laceration in the parietal pleura which may work its way along under the skin as far as the scrotum and upper part of the thigh with tremendous swelling, and the characteristic clinical appearance of subcutaneous emphysema . . . It is rare that air alone is seen in the pleural space as a result of injury to the thorax.' This form is quite different from spontaneous mediastinal emphysema.

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— (1937) *Trans. Ass. Amer. Phys.*, **52**, 311

Lintz, R. M. (1943) *Arch. intern. Med.*, **71**, 256.

Macklin, C. C. (1939) *Arch. intern. Med.*, **64**, 913.

Munroe, D. S., and Webb, G. A. C. (1943) *Canad. med. Ass. J.*, **48**, 232.

MENORRHAGIA AND METRORRHAGIA

See also B.E.M.P., Vol. VIII, p. 508.

Menorrhagia

Treatment

Investigation and methods of treatment—H. J. Stander, C. T. Javert and K. Kuder emphasize the importance of making a correct diagnosis before embarking upon the treatment of abnormal uterine bleeding. Organic causes must first be eliminated by careful examination and, if necessary, by biopsy. In a series of 3,468 cases about 75 per cent were due to an organic cause. In the remaining cases the causes were undetermined in 56.3 per cent, endometrial hyperplasia in 34.8 per cent and irregular endometrial shedding in 8.8 per cent. Twenty patients with functional bleeding of undetermined cause were investigated for deficiencies of vitamins C and K. The vitamin C value and the prothrombin level were found to be below the normal range in 70 per cent and 79 per cent respectively. All the patients with normal figures for either vitamin C or prothrombin levels showed low values for the other. In the treatment of functional bleeding the first step is curettage. In 495 patients observed for more than three years afterwards curettage resulted in cure or in distinct improvement in 71 per cent. Hypofunction of the thyroid gland should be corrected and vitamin deficiencies made good. Subcutaneous injections of snake venom may help in some cases. Irradiation should be reserved for women over childbearing age and hysterectomy, the last resort,

should also be performed only on older women. Endocrine therapy, consisting of successive courses of oestrogen and progesterone, should be tried in younger women.

Progesterone.—G. E. S. Jones and R. W. Te Linde have treated twenty-eight patients with functional uterine bleeding by progesterone. As an initial step curettage was done and hormone therapy was instituted only if severe bleeding recurred. Fourteen patients received one course of progesterone; nine are well; in five amenorrhoea or irregularity resulted. Nine patients required repeated courses; seven are well, in two amenorrhoea or irregular menses developed. Three are still under treatment and are well at present. In two cases hysterectomy was performed, once because treatment failed and once because of associated salpingitis. Some of the patients received progesterone by injection, the rest were given pregnenolone (ethinyltestosterone) by mouth. Of the former, 50 milligrams was given over a period of from seven to ten days each month for four months. Of the latter, the daily dose for seven days was 60 milligrams the first month, 30, 20 and 20 milligrams in the subsequent months. Ill effects were not noted. The cost of the treatment is high, especially when injections are used. The treatment should be reserved for cases in which preservation of ovarian or childbearing function is important.

Metrorrhagia

Treatment

Value of radium.—A paper presented by A. J. Rongy and A. D. Seley at the annual meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons emphasizes the value of radium therapy in selected cases of benign uterine bleeding. The authors have treated 350 patients over a period of fourteen years. The pathogenesis of these conditions is often obscure. Curettage revealed a resting endometrium in 39.3 per cent of this series and endometrial hyperplasia in 45.6 per cent. It is essential that curettage and microscopical examination should precede treatment. In twelve patients in this series unexpected carcinoma of the corpus was thus revealed. Fibroids were present in 285 patients. The decision whether to use radium or to operate in such cases must depend upon the size of the uterus, the location and sensitivity of the tumours, the presence or absence of pain, the sexual history and the operative risk. Complete involution of the tumour after radium treatment occurred in 232 of this series of patients. Patients with submucous, pedunculated or broad ligament fibroids, whether small or large, are never proper subjects for radium; nor should the latter be used if the fibroids are tender. A submucous fibroid, which can be detected by the curette, often undergoes necrosis and infection if treated in this way. A history of pelvic infection or suspicion regarding the presence of pelvic adhesions contra-indicates radium therapy. Operation should be preferred to radium in essential hypertension because of the risk that the induced menopause may further increase blood pressure. The optimum dose was found to be 1800 millicurie hours for women aged forty years of age or more. Nausea and radium burns are less likely to occur when a small dose (25 milligrams) is used over a longer period (seventy-two hours). Occasional sequelae include vesical irritability, leucorrhoea and rectal bleeding, all temporary. Menopausal symptoms are to be expected in about 50 per cent of the patients. Sexual relationship is less likely to be affected by radium than by hysterectomy. The authors estimate that radium can be safely and advantageously used in at least 35 per cent of cases of uterine bleeding.

Jones, G. E. S., and Te Linde, R. W. (1942) *Johns Hopk. Hosp. Bull.*, **71**, 282.

Rongy, A. J., and Seley, A. D. (1943) *Amer. J. Obstet. Gynec.*, **45**, 390.

Stander, H. J., Javert, C. T., and Kuder, K. (1942) *Surg. Gynec. Obstet.*, **75**, 759.

METABOLISM

See also B.E.M.P., Vol. VIII, p. 581.

Metabolism of food constituents

Fat metabolism

Faecal urobilin excretion and blood destruction.—Total urobilin output in the faeces, taken as an index of blood destruction, has been measured by H. W. Josephs, L. E. Holt, Jun., H. C. Tidwell and Charlotte Kajdi in six normal infants, aged from five to eight months, fed on diets containing varying amounts of fat, in order to assess the influence of fats upon the blood. The infants were kept on frames, the faeces were collected and analysed daily and because of the daily fluctuations in urobilin output the average output for two or three days at a time was calculated. An increase in the fat content of the feeds caused a rise in the urobilin output which was approximately equal for all the animal and vegetable fats studied. A similar rise was produced by free fatty acids and soaps. No decrease in the urinary urobilin was observed, hence it was concluded that the action of fat is not to interfere with absorption of urobilin, but to produce haemolysis. An increased excretion of iron in the stools was noted but it was only a temporary rise, possibly because a new equilibrium between excretion and resorption had been attained.

Josephs, H. W., Holt, L. E., Jun., Tidwell, H. C., and Kajdi, Charlotte (1942)
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MOTOR NEURONE DISEASE

See also B.E.M.P., Vol. VIII, p. 611.

Clinical picture*Grouping of cases*

Analysis of symptoms and signs.—Analysis of the records of 197 patients with amyotrophic lateral sclerosis, primary lateral sclerosis and progressive muscular atrophy has led R. L. Swank and T. J. Putnam to the following conclusions. (1) Cases of amyotrophic lateral sclerosis, of which 151 were included in this series, can be divided into three groups, the complete or Charcot type, the incomplete type and the atypical type. Ninety-six cases were placed in the first group; all the patients concerned presented clear evidence of lateral sclerosis, amyotrophy and muscular fibrillation at the first examination. They showed wasting of the muscles of both upper limbs and in some cases of the lower limbs, fascicular twitching in the involved muscles and signs of pyramidal tract disease. Signs of bulbar amyotrophy were observed in forty-five of the patients. In thirty-eight patients the disease was of the incomplete type. They fell into three groups according to the predominance in the clinical picture of lateral sclerosis, amyotrophy or bulbar paralysis. Nine patients showed evidence of rapidly advancing lateral sclerosis with hyperactive reflexes, spastic gait and other signs, and muscular fibrillations were seen in all but one. Five who were kept under supervision until death occurred were known to have developed amyotrophy. Twenty-six patients showed progressive muscular atrophy with fascicular twitchings but no signs of pyramidal tract disease. Three patients showed signs of progressive bulbar paralysis, accompanied in two cases by slight amyotrophy. The atypical group of cases consisted of seventeen patients in whom all the cardinal features of the disease (lateral sclerosis, amyotrophy and muscular fibrillations) were present but the distribution was unusual. Thus in some the manifestations were monoplegic, in others chiefly or entirely confined to the lower limbs; in five cases the atrophic changes began in the proximal muscles of the upper limb and progressed distally. Amyotrophic lateral sclerosis runs a steadily progressive course of from one to six years until its fatal termination is reached. The prognosis appears to increase in gravity as the clinical picture becomes more complete, and with the frequency and magnitude of the muscular fasciculation. Bulbar involvement is always serious. (2) Primary lateral sclerosis without fascicular twitching was observed in twenty-one cases. It is important to recognize this condition, because the expectation of life is much greater than in cases with lateral sclerosis plus fibrillary contractions. (3) Progressive muscular atrophy with few or no fascicular twitchings, of which sixteen cases were included in this series, is distinguished by its insidious onset and slowly progressive course. The prognosis is relatively good.

Swank, R. L., and Putnam, T. J. (1943) *Arch. Neurol. Psychiat.*, **49**, 151.

MOUTH DISEASES

See also B.E.M.P., Vol. VIII, p. 620; and Cumulative Supplement, Key Nos. 1084–1090.

Floor of the mouth*Tumours*

Pathological characteristics of submaxillary salivary gland tumours.—M. B. Dockerty and C. W. Mayo of the Mayo Clinic, where there are approximately five hundred records of tumours of the submaxillary salivary gland, analyse eighty-one cases, all of unilateral lesions. Among the twenty-eight cases in which recurrence took place, practically all the secondary lesions were multicentric masses. Four pathological groups are described as follows. (1) Adenocarcinoma, a mixed type with a rather voluminous stroma containing cartilaginous or myxomatous tissue; this mixed type was present in fifty-one of the eighty-one cases. (2) Fifteen cases of adenocarcinoma of the cylindroma type. (3) An intermediate type between (1) and (2). (4) A miscellaneous group of papillary adenocarcinoma, primary epidermoid carcinoma and other atypical tumours without any of the features of the mixed or the cylindroma types. The average age of the fifty-one patients in the mixed tumour group was thirty-nine years and of the fifteen patients of the cylindroma group eleven were between forty and fifty years of age; in group (3) the average age was forty-nine years; in the miscellaneous group (4) it was forty-four years. Thus the tumours in group (1) appeared ten years earlier than in the other three groups. The duration of the tumours was long, being seven years in the mixed cases when the lesion was primary and from four to seven years when the lesion was a recurrence. In the cylindroma group the average duration was three years, with extremes of six months and six years. Pain may be the only symptom in primary malignant disease of the submaxillary salivary gland.

Jaws*Oro-maxillary fistulae*

Treatment.—D. H. Craig classifies oro-maxillary fistulae due to dental extraction as follows. (1) Temporary, before the mucous membranes of the antrum and of the gums have united: (a) when the antrum is not infected and (b) when the antrum is infected. (2) Permanent, when the fistulae have persisted until union has taken place between the buccal and the antral mucosae: such fistulae vary considerably in size—from quite a large opening, perhaps seven millimetres in diameter, through which the mucosa of the antrum pouts, to an almost

imperceptible orifice from which ooze beads of pus. The fistulae may be situated in the middle of the alveolar ridge or on its lateral side, but not on the medial aspect of the alveolus. Ten cases are reported, to illustrate the two forms of fistulae, the temporary and the permanent. As regards the treatment of temporary fistulae when there is an associated infection of the sinus by irrigation of the antrum through a tooth socket, the author quotes with approval the warning of Voorhees that 'the worst operation in surgery converts a simple condition into chronic suppuration', since irrigation or probing the antrum entails a very considerable risk of such a complication. In the absence of antral infection, it is sufficient to suture together immediately the edges of the gum of the tooth socket, thus supplying a framework upon which the clot can organize and healing can take place. Should the antrum be infected at the time of the extraction of the tooth, or should suppuration supervene in a few days, the antrum should be washed out repeatedly through the inferior meatus of the nose. Before any operation is undertaken for a permanent oro-maxillary fistula, the infected antrum must be treated by an intranasal antrostomy and the antrum should be irrigated through the orifice thus provided until the infection subsides. Technical difficulties arise in the further repair of the fistula, owing to the scar tissue surrounding the fistulous tract; the author describes the operation which was employed in his cases.

Craig, D. H. (1942) *Ulster med. J.*, **11**, 10.

Dockerty, M. B., and Mayo, C. W. (1942) *Proc. Mayo Clin.*, **17**, 593.

MUMPS

See also B.E.M.P., Vol. IX, p. 1; and Cumulative Supplement, Key No. 1092.

Complications

Rare complications

Pre-sternal swelling and oedema of the epiglottis.—C. S. Barker reports that during an epidemic of mumps, three examples occurred among 438 cases of the pre-sternal swelling previously reported by M. J. Radin in 1918. These cases were all in males, aged twenty-eight, twenty-five and nineteen respectively, and in two out of the three the swelling was considerable but it did not appear to be due to cellulitis or to venous obstruction; in one case, however, there was oedema of the epiglottis and of the right lateral wall of the hypopharynx, the sequence of events being somewhat similar to that occurring in Ludwig's angina.

Barker, C. S. (1943) *Canad. med. Ass. J.*, **48**, 22.

Radin, M. J. (1918) *Arch. intern. Med.*, **22**, 354.

MUSCLE DISEASES

See also B.E.M.P., Vol. IX, p. 11; and Cumulative Supplement, Key Nos. 1093–1099.

Injuries

Indirect

Hernia of the tibialis anterior muscle.—I. D. Kitchin and D. A. Richmond record, with three illustrations, the occurrence of a hernia through the fascia over the tibialis anterior muscle, all the cases concerning soldiers who had had strenuous exercise in rough country. The lesions were first regarded as small varicose veins; they were small, about the size of peas, all could be reduced and the splits in the fascia over the tibialis anterior were easily felt. The hernias were not tender, and disappeared completely on pressure and when the muscle was contracted. References are given to seventeen cases in Alpine soldiers (H. Ihde; A. A. Schmier), but the condition is seldom recognized.

Myositis

Classification

Acute myalgia of the neck and shoulders.—P. Beeson and T. F. McN. Scott describe their observations, made with the assistance of trained public health nurses in England during the winter of 1941–2, on several cases of acute myalgia of the neck and shoulders occurring among members of the staff of the Red Cross Harvard Field Hospital Unit. Similar cases also occurred in four outbreaks in the same district, amounting to a total of 125 persons affected. The condition, giving rise to a typical stiff neck or acute torticollis, was described in the United States of America in 1935 by B. E. Massell and R. Solomon. Usually the disease is of short duration. In fifty-two patients it lasted for four days and ended with complete recovery but, in about 15 per cent, the pain and stiffness persisted for weeks and occasionally the condition passed into generalized fibrositis. The trapezius muscle was involved in nearly all the cases, which thus differed from those seen in Bornholm disease and from so-called epidemic myositis in which that muscle is seldom involved. After the trapezius muscle the deltoid muscle and the muscles of the scapula are most often affected; the sternocleidomastoid muscle is rarely the site of pain, which is bilateral. Headache occurred in about half of the number of cases. Tenderness was found in the acute phase, but in only 55 per cent of cases was it the cause of complaint. In many cases nodules could be felt in the affected muscle and disappeared under the influence of heat and massage; they were probably caused by muscular spasm; other nodules, however, were more persistent and may have been fibrositic. Fever was not characteristic of the disease although, in severe cases, the temperature might reach 100° F.

The leucocyte count was usually within normal limits but there was often a moderate lymphocytosis. The authors found that in fifty-one of the 125 patients, or 41 per cent, the common cold coincided with the onset of the disease. The transmission of the disease was investigated experimentally by inoculation of mice, guinea-pigs and rabbits with washings from the nose and throat of patients with myalgia, and of human volunteers by intranasal spraying with nasal washings and by inoculation with whole blood from infected persons. The evidence for experimental transmission of the disease is not complete; the disease could not be produced in the experimental animals, but injection of whole blood from acute cases appeared to give positive results, although they were not conclusive because of the prevalence of the disease in the community at the time. The incubation period appeared to be from two to four days. Bacteriological examination of the throat did not throw any light on the aetiology but the probability of an infection was accepted. The disease may occur in epidemics, but it is not Bornholm disease which is accompanied by characteristic pleuritic pain and leucocytosis, and seldom by pain in the trapezius muscle. Recently other epidemic diseases have been described under titles which suggest a possible identity with the cases which have been recorded by Beeson and Scott; these are epidemic myositis with neuritis, erythema and meningeal symptoms (D. Williams), and brachial neuritis in epidemic form (R. Wyburn-Mason). L. E. Houghton and E. I. Jones also described cases of persistent myalgia which developed after a sore throat.

Morbid anatomy

Polymyositis.—D. Goldman reports a case which during life had been regarded as one of atypical bulbar paralysis and was found at necropsy to show widespread changes microscopically in the skeletal muscles. There was fragmentation of the muscle fibres which also showed hyalinization, degeneration, loss of striation, increase of nuclei and extensive infiltration with lymphocytes, monocytes and polymorphonuclear leucocytes. The report of the neuropathological laboratory was 'chronic cell change' in the medulla and cerebral cortex. The myocardium showed arteriosclerosis and arteriolosclerosis, but none of the degenerative changes present in the skeletal muscles. The patient was a Jew, aged sixty-three, who was ill for two years before his death. The neuropathological changes were regarded as being secondary to those in the skeletal muscles.

Beeson, P., and Scott, T. F. McN. (1942) *Proc. R. Soc. Med.*, **35**, 733.

Goldman, D. (1942) *Arch. intern. Med.*, **70**, 822.

Houghton, L. E., and Jones, E. I. (1942) *Lancet*, **1**, 196.

Idhe, H. (1929) *Acta chir. scand.*, **65**, 97.

Kitchin, I. D., and Richmond, D. A. (1943) *Brit. med. J.*, **1**, 602.

Massell, B. I., and Solomon, R. (1935) *New Engl. J. Med.*, **213**, 399.

Schmier, A. A. (1937) *J. Amer. med. Ass.*, **109**, 28.

Williams, D. (1941) *Quart. J. Med. N.S.*, **10**, 287.

Wyburn-Mason, R. (1941) *Lancet*, **2**, 662.

MYASTHENIA GRAVIS

See also B.E.M.P., Vol. IX, p. 34; and Cumulative Supplement, Key No. 1100.

Morbid anatomy and pathology

Cardiac lesions

Myocardial changes.—The association of myasthenia gravis with diffuse myocardial lesions is reported by A. Rottino, R. Poppiti and J. Rao. The patient, a fifty-four-year-old woman, was admitted to hospital complaining of progressive weakness of two years' duration and of attacks of dyspnoea, simulating asthma, for the last six days. Dysarthria, ptosis of one lid and weakness of the extremities were present. A few crepitations were heard at the bases of the lungs. The cardiac sounds were poor, the heart was not enlarged and the rate was 130 with frequent extrasystoles. Death took place four hours after admission. At necropsy the outstanding findings were a thymic tumour weighing 45 grammes; slight enlargement of the spleen; benign cortical adenoma of one suprarenal gland; mild oedema of the lungs. The myocardium was somewhat pale and on section showed diffuse infiltration and oedema, occasional small haemorrhages and fragmentation of many myofibrils. The exudate consisted mainly of large irregular cells with scanty cytoplasm. In the endocardium small elevations, formed by similar cells, were present. The skeletal muscles showed many small nests of lymphocytes. In a second classical case of myasthenia gravis myocardial lesions were not found. The authors are unable to decide the relation between the myocardial condition and the myasthenia in the first patient.

Rottino, A., Poppiti, R., and Rao, J. (1942) *Arch. Path.*, **34**, 557.

MYOPIA

See also B.E.M.P., Vol. IX, p. 66.

Treatment

Management of different clinical types

Calcium and vitamin D.—Opening a discussion on myopia at a meeting of the American Academy of Ophthalmology and Otolaryngology, A. Cowan questioned Donders's dictum

that every myopic eye is unsound, and expressed a wish that the terms malignant, pathological and pernicious myopia might be abolished. These terms indicate some disease either that occurs in a myopic eye or that happens to result in myopia. The speaker had never seen a case in which simple myopia in a healthy eye developed into the so-called malignant type. The management of myopia depends upon whether the case is one of a simple anomaly of refraction or one of a disease. Provided that evidence of disease is absent and that visual acuity is normal, simple myopia of any degree should be treated as a form of ametropia no more serious than any other. Its development cannot be prevented or retarded, and treatment should be by full correction and repeated adjustment, without restriction of the use of the eyes. E. C. Ellett reported that a few women who were observed for some forty years and who wore their glasses very little, were not any worse off in the end than others who had constantly worn their glasses. It is impossible to say which cases will progress or to prevent progress occurring. In 103 cases in which adrenaline (epinephrine) was prescribed, a noticeable retarding effect was not observed. A. A. Knapp related his experiences with animals, in which myopia was induced by a diet deficient in calcium and in vitamin D, and shrinkage of the eyeball resulted after these substances had been administered. Clinically, shrinkage of the posterior segment of the eye, which was measured by photography, was observed in a myopic subject who was treated by calcium and vitamin D; and the condition of 50 per cent of myopic eyes remained stationary with such treatment. S. R. Gifford deprecated the practice of placing children with simple myopia in sight-saving classes, a view with which Cowan, winding up the discussion, agreed; the latter cast doubt on Knapp's conclusions, pointing out that about 50 per cent of cases of myopia remain stationary without any treatment at all.

Cowan, A., Ellett, E. C., Knapp, A. A., and Gifford, S. R. (1942) *Amer. J. Ophthalm.*, 25, 844

MYXOEDEMA

See also B.E.M.P., Vol. IX, p. 69.

Clinical picture

General signs and symptoms

Pretibial myxoedema in thyrotoxicosis—W. R. Trotter and K. C. Eden record four cases (male one, females three) of localized pretibial myxoedema, and analyse seventy-three collected recorded cases. The condition has come chiefly under the notice of dermatologists; of forty-five journal records of cases of localized pretibial myxoedema, thirty-four appeared in dermatological journals. Not a single case of localized pretibial myxoedema has been described in a patient who was without past or present thyrotoxicosis; generally, although not invariably, the condition develops when the patient is actively thyrotoxic, and it is not affected by the administration of thyroid extract or by thyroidectomy. It does not seem, therefore, to be the direct result of either hypothyroidism or thyrotoxicosis. The condition occurs most often in subjects who are between twenty and forty years of age. There is a group of cases in which localized myxoedema is not present over the tibiae but may be present in any other part of the body. The cases without localized pretibial myxoedema are divided into (1) those with hypothyroidism, which are the more numerous, and (2) those in which hypothyroidism is not present; very few cases belong to the second group. Histologically it has been shown that the skin which is affected in pretibial localized myxoedema contains mucin.

Types of anginal pain—Several types of anginal pain occurring in patients with myxoedema are described by A. A. F. Peel. (1) Angina of effort was seen in twelve patients. Ten had some form of heart disease as well as myxoedema. In five of the patients, four with independent heart disease, the anginal attacks began during treatment with thyroid gland extract. In others, thyroid extract sometimes alleviated and sometimes had not any effect upon the pain. For many patients an optimum dose exists above which pain returns. (2) Two examples of Zondek's 'abortive myxoedema heart' were observed; the patient concerned complained of continuous praecordial distress with intermittent attacks of collapse. Treatment by thyroid extract brought complete relief. (3) Spasmodic anginal attacks occurred in two patients. One had a low sugar tolerance curve and was treated with glucose and thyroid with complete relief. The other's haemoglobin was only 75 per cent and the attacks ceased when it was increased to 92 per cent by iron therapy.

Peel, A. A. F. (1943) *Brit. Heart J.*, 5, 89

Trotter, W. R., and Eden, K. C. (1942) *Quart J. Med. N.S.*, 11, 229

NAILS, DISEASES OF

See also B.E.M.P., Vol. IX, p. 83.

Nails as a health signal

W. D. Langley and O. A. Gordon review the common changes seen in the nails, comparing them with the hair as occasionally sign-posts of systemic disease and also of certain occupations; for example, reference is made to the discoloured nails of the surgeon who uses Harrington's (mercurial) solution as a pre-operative preparation for the skin of his hands; in the same group are cases comprising baffling manifestations caused by the various processes of modern manicure, polish or polish remover. Anatomically the nail is formed by an epidermal invagina-

tion and in longitudinal section is composed of the following structures: at the tip of the invagination lies the nail matrix, from which the nail is produced. Its cells grow distally and undergo cornification. The anterior part of the matrix is visible through the posterior portion of the nail plate as a convex crescentic surface called the lunula. The plate grows continuously throughout life, the rate of growth being approximately 1 millimetre a week, but this varies with age, fingers or toes and seasons of the year. If a plate is damaged or partially destroyed, it will usually regenerate. If the matrix is destroyed, there will not be any regeneration of the plate. Longitudinal striation of the nail plate, with or without fissures, is known as onychorhexis; this is common especially in old people without any other pathological symptoms; it may be associated with eczema, psoriasis, fungous infection, leprosy and lichen planus. Defects in the nail plate running transversely are called Beau's lines; they occur after severe illnesses, injury to an extremity, childbirth, eczema, psoriasis, and are found especially on the great toe nail. Leukonychia, the presence of 'white spots' on the nail plate, is one of the common phenomena observed. Among a hundred normal persons P. L. Singer found 58 per cent in men and 75 per cent in women. An uncommon congenital defect of the nails is complete absence of most of the nails (anonychia) and the others rudimentary nails. A group of nail changes is connected with the ungual manifestations of the dermatoses; in this the authors give psoriasis the first place.

Langley, W. D., and Gordon, O. A. (1943) *Bull. Guthrie Clin.*, **12**, 143.

Singer, P. L. (1931) *Arch. Derm. Syph.*, N.Y., **24**, 112.

NEMATODE INFECTIONS, INTESTINAL

See also B.E.M.P., Vol. IX, p. 125; and Cumulative Supplement, Key Nos. 1126-1130.

Oxyuriasis

General prevalence of threadworm infestation

In negro and in white children.—Eugenia C. Jones has studied the incidence of pinworm (threadworm) infestation in sixty white and sixty negro children admitted to hospital for various medical and surgical conditions. Specimens were taken by the N.I.H. swab method on alternate nights between 11 p.m. and 1 a.m., when the children had been asleep for at least two hours. It was not always possible, owing to the short periods in which the children were in hospital, to secure the four swabs which are considered the least number for reliable results. The average number of swabs taken from each child was 2.9, and at least four were taken from each of forty-five children. Oxyuriasis was discovered in fifteen white and two negro children, that is the incidence of infection was 25 per cent among the former 3 per cent among the latter. Both the infected negro children were boys in the six to twelve year age group. In the white group the sexes were affected equally. The results confirm reports of a lower incidence of threadworm infestation in negro than in white children. The total incidence is lower than has been found in previous studies of the general population. The author suggests that hospital procedures such as the giving of enemas and the taking of temperatures in the rectum may have influenced the result.

Incidence and diagnosis

The Cellophane swab test.—May R. Young has determined the incidence of threadworm infestation in 119 children in Cell Barnes (St. Bartholomew's) hospital and in forty children in a London resident nursery school. The diagnosis may be made either by seeing the worms migrating or in the stool, or by finding ova in the faeces or in material obtained by means of the Cellophane anal swab. This swab, designed by Hall in 1937, consists of a piece of Cellophane an inch square folded over the rounded end of a glass rod and fixed by a rubber band. Considering the high incidence in children, the finding of worms in the stools is rare and examination of the stools for ova by the zinc sulphate concentration flotation method is much less effective than by the use of the Cellophane swab. Only 5 per cent of the hospital group of 119 children showed ova in the stools, of which three per cent were examined by the zinc sulphate concentration flotation method, whereas 21.8 per cent gave positive results on examination by one Cellophane swab, 33.6 per cent with two swabs and 42 per cent with three swabs. American workers have shown that seven swabs per individual permits detection of 99 per cent of the total number of persons infested. In the nursery school group of forty children examination by two swabs per child showed infestation in 55 per cent. American workers insist that strict hygiene must accompany treatment.

Threadworms in children

Typical symptoms.—A. Moncrieff, summarizing recent work on threadworms in children, thinks that the work of T. E. H. Weller and C. W. Sorenson strongly suggests that threadworms do not cause any symptoms in the majority of cases. Over 500 children, none of whom was known to be harbouring threadworms, were examined by Weller and Sorenson. Examination was by Cellophane (N.I.H.) swabs and 19 per cent of the children were found to be infested. The incidence of three groups of symptoms popularly attributed to threadworms was also studied by the authors. The symptoms selected were (1) gastro-intestinal, such as nausea and vomiting, abdominal pain, diarrhoea, loss of weight and alterations in appetite; (2) local, such as anal pruritus and skin lesions, vulvitis and vaginitis; and (3) nervous, such as nocturnal restlessness, enuresis and masturbation. The results showed that, among the children with threadworms, there was no higher incidence of the gastro-intestinal

symptoms, except that, contrary to popular belief, their appetite was less than that of the non-infected children. The incidence of vulvitis and of nocturnal restlessness was similar in both infected and non-infected children. The slight increase of the other local symptoms and of enuresis and masturbation among the infected children was not statistically significant. The best means of diagnosis are the observation of worms in the neighbourhood of the anus at night and the use of the special swab. The prevalence of threadworm infestation among children attending hospital for quite different complaints points to a relatively high incidence in the general population. It is useless to cure the individual patient unless home and school contacts are also dealt with. For the detection of these the swab must be used; symptoms cannot be relied upon. Recent evidence strongly suggests that phenothiazine is much too dangerous for general use. The best remedy at present available is, in the author's opinion, gentian violet given in special capsules. The treatment recommended is a dose of $\frac{1}{4}$ grain (10 milligrams) per year of age per day for five days, five days' rest, then another five-day course of gentian violet.

Treatment

Fatal phenothiazine poisoning.—D. R. Humphreys reports a fatal case of phenothiazine poisoning. The patient, a girl aged six, was admitted to hospital because of pallor and vomiting. Eleven days previously she had been taken to the doctor with anal irritation; he had diagnosed threadworm infestation and had prescribed 2 grammes (30 grains) of phenothiazine daily. On the fourth day of treatment the child looked rather pale. On the fifth day she was tired and a little yellow, and was given only 1 gramme on this and on the next day. On the eighth day vomiting began, and the child was kept in bed until she was admitted to hospital three days later. On admission she was pale and slightly jaundiced; the temperature was 102.4° F. The blood count showed only 1,250,000 erythrocytes and 26 per cent haemoglobin. The next day the patient was given 300 cubic centimetres of blood by drip transfusion over a period of three hours. Half an hour later she had a rigor and the temperature rose to 106.8° F. She was given fluids and alkalis in large doses, but became comatose and died eleven hours after the transfusion. No threadworms were passed while the child was in hospital, and none was found at necropsy, at which the appearances observed were characteristic of acute haemolytic anaemia, without evidence of toxic hepatitis or of nephritis. The author does not mention what precautions were taken to ensure compatibility of the transfused blood but it is clear that some degree of incompatibility was present, and the resulting reaction in so anaemic a subject may well have been the determining cause of death.

Successful results with gentian violet.—Eloise B. Cram summarizes the conclusions of studies on oxyuriasis carried out by various workers under the auspices of the United States Public Health Service. The life cycle of *Oxyuris vermicularis* has not been elucidated but it appears that female worms first leave the anus from fifteen to twenty-eight days after the ova enter the host's body. They proceed to deposit the ova on the skin, each worm producing roughly 11,000 eggs. Dust from the homes of infected people has been shown to contain ova. In cool, moist conditions few ova fail to hatch after forty-eight hours. Faecal examination is inadequate for diagnosis. Swabbing with a special cellophane swab is much surer, but often needs to be repeated. The incidence of oxyuriasis in different groups of people averaged 41.5 per cent for white people and 12.9 per cent for negroes. Infection is frequently found in more than one member of a family. Symptoms and signs observed were itching, restlessness and insomnia, slight eosinophilia and in some people gastro-intestinal disturbances. If constant reinfection is to be avoided treatment must be given to every infected member of a household. Gentian violet was found to give better results than any other anthelmintic.

Cram, Eloise B. (1943) *Amer. J. Dis. Child.*, **65**, 46.

Humphreys, D. R. (1942) *Lancet*, **2**, 39.

Jones, Eugenia C. (1942) *Amer. J. Dis. Child.*, **64**, 803.

Moncrieff, A. (1942) *Practitioner*, **149**, 216.

Weller, T. E. H., and Sorenson, C. W. (1941) *New Engl. J. Med.*, **224**, 143.

Young, May R. (1942) *Proc. R. Soc. Med.*, **35**, 684.

NEPHRITIS AND NEPHROSIS

See also B.E.M.P., Vol. IX, p. 134; and Cumulative Supplement, Key Nos. 1131–1141.

Aetiology

Glomerulo-nephritis

Prophylaxis by tonsillectomy.—J. D. Lyttle discusses afresh the question whether or not tonsillectomy exerts any prophylactic influence on the occurrence of nephritis due to streptococcus infection, chiefly of the upper respiratory tract. He points out that the type of infection in nephritis is quite different from that in rheumatic fever; instead of a mild evanescent sore throat such as that which precedes the rheumatic attack, the child with nephritis has a deep infection such as adenitis in the neck or mastoiditis, and nephritis is found on routine examination. There is not any evidence that tonsillectomy plays any important part in the prevention of acute nephritis; in the author's series at the Babies' Hospital about one-third of the cases of acute glomerulo-nephritis had undergone tonsillectomy. The object of tonsillectomy is presumably the prevention of chronic nephritis by removal of a focus of infection.

The author has never been convinced that an attack on a septic focus has influenced the course of the disease when chronic nephritis has become established. He recommends, however, that if any of the generally accepted indications for tonsillectomy are present in a case of either acute or chronic nephritis, the operation should be carried out.

Morbid anatomy

Glomerulo-nephritis

Acute and chronic lesions.—H. A. Christian emphasizes the non-specific character of glomerular lesions of the kidney. The majority of those which have been observed are to be regarded as inflammatory. Injury is followed by degenerative changes and these in turn initiate proliferative changes. Further degeneration often succeeds proliferation. Finally reparative processes may appear. The proliferative changes are seen either in the capillary endothelium or in the capsular epithelium, and of the latter either the parietal or the visceral layer may be most affected. Thrombosis may occur in the capillaries of the glomerular tuft. If the lesions become chronic the glomeruli show various stages of atrophy and fibrosis before they finally disappear. These changes have been found by the author in acute and subacute glomerulo-nephritis, subacute bacterial endocarditis, acute and subacute pyelonephritis and uranium poisoning, and account for the many similarities in the signs and symptoms of different forms of renal disease, irrespective of its cause.

Histological changes.—At the Annual Session of the American Medical Association J. P. Simonds discussed changes in the kidney which are brought about by disease. Each kidney is made up of about a million nephrons consisting of a glomerulus concerned with filtration, and a tubule in which selective reabsorption occurs. The total blood flow to the kidney is very great and nearly all of it passes through the glomeruli and then through a peritubular capillary system. Any factor which reduces the flow of blood through the glomeruli will both decrease filtration and, by diminishing the blood supply to the tubules, interfere with concentration of the filtrate. The pressure falls steeply between the glomerular and the peritubular capillaries. In the glomeruli the pressure is sufficient to overcome the osmotic pressure of the plasma proteins. In the peritubular capillaries not only is the hydrostatic pressure decreased but, owing to the loss of water from the blood by filtration in the glomeruli, the osmotic pressure is high, thus the direction of flow of fluids is towards the blood stream. To ensure an adequate volume of filtrate enough blood must pass through healthy glomeruli. The two chief pathological conditions which interfere with this process are sclerosis of the afferent arterioles to the glomeruli and disease of the glomeruli themselves. The former is found in chronic hypertension, the latter in glomerulo-nephritis. In hypertension functional vasoconstriction occurs first. The resultant production of renin increases spasm and so initiates a vicious circle. The next stage is characterized by hypertrophy of the muscular coat, and finally the walls of the arterioles are transformed into narrow hyaline tubes which are incapable of dilatation. In glomerulo-nephritis injury to the glomeruli results in increased permeability, allowing the escape of serum albumin, and tubular damage causes loss of concentrating power. Renal insufficiency with retention of waste products and uraemia is the final outcome of glomerular destruction.

Relation of nephritis to hypertension

Morbid anatomy

Incidence of pyelonephritis and hypertension.—N. M. Shute, in order to correlate the incidence of pyelonephritis and hypertension, analyses the data of the 11,898 necropsies made during the ten years 1930-9 inclusive at the Cook County Hospital. The connecting link between the two conditions as shown by the experimental work of H. Goldblatt and other workers, has been confirmed by numerous clinico-pathological observations, such as those of S. Weiss and F. Parker, Jun., on the presence of prominent vascular changes in the kidneys, especially in the chronic and healed cases. Among the 11,898 necropsies there were 290 cases or 2.5 per cent of pyelonephritis; of these 224 or 77 per cent were bilateral, and 66 were unilateral. There were 160 males and 130 females, or 55.2 and 44.8 per cent respectively. The criteria of hypertension were a systolic pressure of 150 and a diastolic pressure of 95 millimetres Hg. The incidence of hypertension among the 290 cases, regardless of sex, age and race, was 44.4 per cent. The cases with hypertension were divided into six age groups:

AGE GROUPS	HYPERTENSION PERCENTAGE	RENAL VASCULAR PERCENTAGE
Under 30 years	28	29
31-40	33.3	33.3
41-50	41	49
51-60	49	56
Over 60	63	69

The predominance of males in the total number of cases of pyelonephritis and hypertension was mainly in the older age groups. Although it was not possible to divide the cases of pyelonephritis into acute, chronic and healed forms, young women probably died in the acute stages. Patients with bilateral pyelonephritis showed a higher incidence of hypertension than did those with unilateral pyelonephritis.

Vascular phase of chronic diffuse glomerulo-nephritis.—H. Horn, P. Klemperer and M. F. Steinberg, in a clinico-pathological investigation, analyse forty-nine consecutive cases of chronic diffuse glomerulo-nephritis selected from those seen during the period 1st January, 1927 to 1st July, 1938 from a total of 5,232 necropsies. The investigation deals with the questions of malignant hypertension and arteriolo-necrotic lesions in patients with chronic diffuse glomerulo-nephritis. Morphologically microscopical examination was made of the kidneys, pancreas, adrenal glands, testes, myocardium and all other available organs, and clinically the features, especially the blood pressure, were reviewed separately. Each case was then classified as (1) slowly progressive arteriosclerosis (fourteen cases), (2) transitional accelerated arteriosclerosis (thirteen cases) and (3) advanced accelerated arteriosclerosis (twenty-two cases). The above three groups presented striking histological differences. (1) The slowly progressive or 'negative' type showed slight to occasionally severe thickening of the intima in the interlobular arteries, and the larger arteries showed slight or moderate hyperplasia of the internal elastic membrane and often fibrillar disruption, and the arterioles, including the vasa afferentia, presented hyalinized walls and fatty change and encroachment in the lumen. (2) The transitional accelerated form is characterized by cellular proliferation within the intimal layers of the interlobular arteries. Arteriolo-necrosis is not seen in this form. (3) In the advanced accelerated form the cellular proliferation is even more prominent, and the arterioles may be obliterated. Males are more numerous in the advanced accelerated cases in which the systolic blood pressure reached 200 millimetres Hg in 73 per cent. In both the transitional and the advanced accelerated groups the retinal changes and the necrotic changes in the arterioles are characteristically present, thus contrasting with the slowly progressive group in which they do not occur. The anatomical changes in groups (2) and (3) correspond with the clinical features of malignant hypertension.

Christian, H. A. (1942) *Amer. J. med. Sci.*, **204**, 781.

Goldblatt, H. (1938) *Bull. N. Y. Acad. Med.*, **14**, 523.

Horn, H., Klemperer, P., and Steinberg, M. F. (1942) *Arch. intern. Med.*, **70**, 260.

Lyttle, J. D. (1942) *Bull. N. Y. Acad. Med.*, **18**, 356.

Shure, N. M. (1942) *Arch. intern. Med.*, **70**, 284.

Simonds, J. P. (1942) *J. Amer. med. Ass.*, **120**, 89.

Weiss, S., and Parker, I., Jun. (1939) *Medicine, Baltimore*, **18**, 221.

NERVE INJURY AND REPAIR

See also B.I.M.P., Vol. IX, p. 160.

Causes of nerve injury

Severing of nerve

Repair of divided nerves by fibrin suture—H. J. Seddon and P. B. Medawar report results obtained when fibrin is used to repair divided nerves. One case of recent injury and fourteen cases, in all of which secondary suture or grafting was required, are included. In cases of long standing, the nerve endings are always separated by a considerable gap, and often they can be approximated only under tension or in some unnatural position. Such lesions are unsuitable for plasma suture. Differences in diameter of the two endings depend upon the length of time which has elapsed since the injury, careful suturing is necessary, plasma alone not being of any use. Retraction of the sheath also takes place and may necessitate the insertion of stitches. The conditions necessary for fibrin suture are as follows. (1) Absence of tension at the suture line. (2) No great disparity in area of the cut surfaces. (3) The possibility of placing the cut endings in a small pool in which plasma can collect and set. Bone wax can sometimes be used to form a cup. Plasma may be useful when the nerve endings are in an inaccessible position. It may be possible to insert a few stitches somewhat apart from the suture line to anchor the stumps, to lay the cut surfaces in contact and to seal them with plasma. For grafting, fibrin suture is invaluable but it remains to be seen whether or not grafting is worth while. The authors claim, not that the results of fibrin suture are better than those obtained by stitching, but that it has great technical advantages over older methods. Concentrated plasma can be prepared in any pathological laboratory.

Morphological changes resulting from nerve injury

Microscopical changes

Adjustments of nerve endings.—In a Harvey lecture in January, 1941 C. C. Speidel, Professor of Anatomy in the University of Virginia, reviews the work of S. Ramón y Cajal and R. G. Harrison on tissue culture methods, and discusses his own researches on the growth of individual nerve sprouts, the movements of neurilemma cells and the process of myelination in experimental sheath formation. He also reviews recent work, not yet published, on the experimental production of changes in nerve endings associated with alterations in normal and experimental conditions, growth, retraction, irritation and degeneration, and on the results of shock therapy and insulin treatment. These extensive observations, well illustrated here by nineteen diagrams, were made mainly on living tadpoles. Thus the first figure shows the appearances, not only of the ordinary nerve endings in the resting stage, but also of those in stages of growth, retraction, irritation and degeneration. The phenomena of extension and retraction are seen best in the tips of young or rapidly regenerating nerve fibres. Young

tadpoles are especially responsive to alternating periods of starvation and good nutrition. Tadpoles immersed in weak solutions of alcohol or chlorotone (chlorbutol) become slightly dazed, and their nerve fibres and nerve endings show pronounced changes. Myelinated fibres are vacuolated; they also show fibrillation of the axis cylinder, swelling, progressive separation of the axis cylinder and myelin sheath, globule formation and, in extreme cases, complete degeneration of some myelin segments with or without degeneration of the corresponding length of axis cylinder. Starvation induces regressive changes of swelling, retraction and degeneration. Alternate retraction and growth of the same individual nerve ending may be induced experimentally by imposing on tadpoles alternating periods of starvation and good nutrition. During regeneration after injury, nerve fibres and their branches duplicate an original pattern only as far as they are ensheathed by the original neurilemma. The changes in irritated or slightly injured nerve endings which will recover resemble closely the early changes in nerve endings, undergoing trophic degeneration which will not recover. Free nerve endings, present in large numbers in the central nervous system, probably undergo adjustments similar to those of free peripheral and cutaneous nerve endings. Synaptic changes would therefore be possible in the brain and in the patterns of synaptic mechanisms, which might be set up as the result of shock treatments, severe intoxications and fevers, and severe nutritional or hormonal imbalance.

Symptoms of nerve injury

Motor disturbances

Recovery of motor functions after injury.—Little reliable information is yet available about the factors influencing recovery of motor function after nerve lesions. E. Gutmann has endeavoured to add to the stock of knowledge by studying recovery of function in the rabbit after lesions of the peroneal nerve. Certain processes have to take place in a nerve before functional continuity is restored, even after many of its fibres have made connexion with the periphery and the muscle responds to electrical stimulation of the nerve. Indirect electrical excitability is therefore not a true test of physiological recovery. In testing for the latter, advantage was taken of the fact that in the rabbit a reflex is present causing spreading of the second, third and fourth toes when the animal is held up by the loose skin of the back and then suddenly lowered. This reflex is served by the peroneal nerve. This nerve was interrupted by operation, either by crushing at one point, crushing over a considerable length, division followed by plasma suture or division followed by suture with silk. Paralysis follows, characterized by drop foot and absence of the spreading reflex. When the nerve is interrupted by crushing at the level of the knee, fibres first reach the muscle about ten days after the injury. Contraction on stimulation of the nerve appears after about eighteen or twenty days. The first sign of reflex function is observed after about twenty-five days and complete function eight days later. For a time after recovery the reflex may show increased amplitude. The chief factors which were found to affect recovery were as follows. (1) The level of the nerve lesion, which in different sets of experiments was situated at various distances from the muscle. The higher the lesion the longer the period between arrival of fibres at the muscle and complete restoration of function. This may be due in part to the greater degree of muscular atrophy associated with the more distant lesions. The rate of regeneration of the nerve is not slower with the higher lesions. (2) The type of injury. Recovery is most rapid when the nerve is crushed at one point, slower when a considerable length is crushed and slowest after complete division and suture. The reason may be found in the existence of difference in the amount of scar tissue formed. (3) Recovery is slowed if a gap is left in the nerve. (4) Recovery after a second crush occurs more quickly than after the initial crushing, provided that a sufficient interval (at least sixteen days) elapses between the injuries. (5) The rate of recovery is reduced by delay in suture. Recovery of motor function is obviously a complex process, not a matter merely of outgrowth of axones.

Gutmann, E. (1942) *J. Neurol. Psychiat.*, **5**, 81.

Harrison, R. G. (1910) *J. exp. Zool.*, **9**, 787.

— (1914) *ibid.*, **17**, 521.

Ramón y Cajal, S. (1928) *Degeneration and Regeneration of the Nervous System*, London.

— (1933) *Histology*, London.

Seddon, H. J., and Medawar, P. B. (1942) *Lancet*, **2**, 87.

Speidel, C. C. (1942) *Bull. N.Y. Acad. Med.*, **18**, 625.

NEURITIS

See also B.E.M.P., Vol. IX, p. 182.

Multiple neuritis

Aetiology

Nerve paralyses after local sulphonamide application.—Because nerve paralyses have often occurred after systemic administration of sulphonamides, W. Holmes and P. B. Medawar, arguing that the toxic effect on nerves would probably be more pronounced when the drugs were applied locally, have investigated their action upon the exposed intact sciatic nerve of the rabbit. Sterile sulphanilamide was packed along the nerve for a distance of about four centimetres. The animals were divided into two groups, one receiving 1 gramme (15 grains),

the other being given 2 grammes (30 grains) of the powder. When tested twenty-four hours later, the animals of the first group showed neither motor nor sensory disturbances; those in the second group were insensitive to pinprick over the whole of the corresponding foot and had lost the power to spread the toes. Fifteen days later specimens of nerve were removed from animals of both groups and were examined histologically. In the first group the sections showed no changes; in the sections from the second group degeneration both of the axones and of the myelin sheaths was apparent, and macrophages and Schwann cells were much less abundant than they are when degeneration occurs after section of a nerve; but in specimens of nerve removed after sixty days regeneration was nevertheless proceeding normally. The authors advise caution in the use of sulphonamides in the vicinity of nerve trunks; their experiments show that the toxic effect, although feeble, is not negligible.

Holmes, W., and Medawar, P. B. (1942) *Lancet*, 2, 334.

NYSTAGMUS

See also B.E.M.P., Vol. IX, p. 263; and Cumulative Supplement, Key Nos. 1169–1173.

Miners' nystagmus

Treatment

Prophylaxis by illumination.—W. J. W. Ferguson describes an experiment with stronger lighting in mines in an attempt to ascertain the minimum amount of illumination necessary to abolish miners' nystagmus. In each colliery one shift was equipped with higher powered lamps and one control shift with ordinary lamps. The difference between the lamps was 2–2½ candle power. The men were examined at six-monthly intervals over a period of three years. The number showing nystagmus at the beginning of the experiment was twelve in each shift. At the end of the experiment the control shift showed sixteen instances of nystagmus, the other shift only five.

Ferguson, W. J. W. (1943) *Brit. J. phys. Med. N.S.*, 6, 40.

OESOPHAGUS DISEASES

See also B.E.M.P., Vol. IX, p. 287; and Cumulative Supplement, Key Nos. 1176–1188.

Tumours

Non-malignant

Multiple polypi.—R. Dickes, A. F. Knudsen and S. C. Franco record the rare condition of multiple 'polypi' of the oesophagus with massive gastro-intestinal haemorrhages. The history of the patient—a girl, aged seven—went back to 1928 when she had had jaundice, abdominal distension and enlarged veins on the abdominal wall. A diagnosis of Banti's syndrome and of oesophageal varices was made in 1935 and splenectomy was performed with some temporary benefit; pieces of the liver and spleen were taken for biopsy and showed evidence of slight chronic inflammation and cellular degeneration. In 1937, 1938, 1939 and 1940 the symptoms recurred. In the last of these years oesophagostomy showed the presence, in the lower third of the oesophagus, of pale glistening projections of irregular size but sufficiently large to occlude the lumen; they were regarded as 'polypi'. Oesophagostomy was repeated and a specimen taken for biopsy; this procedure was at once followed by a copious gush of blood. Histologically the projections of the oesophageal mucosa showed thickening but not any downgrowth of the squamous epithelium; numerous blood channels were present in the mucosa. But the pathologist could not diagnose oesophageal 'polypi'. Finally, repeated treatment of the thickened areas by fulguration resulted in cure.

Malignant

Surgical treatment.—G. G. Turner sets out a reasoned case for early diagnosis and surgical treatment of primary carcinoma of the oesophagus, and quotes a chance remark of the late William Mayo, made while he was performing a gastrotomy thirty-six years ago, that it was 'always worth while to perform this operation because the diagnosis might be wrong'. Since then Turner has seen several cases in which the more serious view, although confidently expected, proved to be too pessimistic, and has not any hesitation in stating that in cases of cervical carcinoma of the oesophagus without invasion of the surrounding tissues and lymphatic glands, well planned surgical intervention holds out a much better prospect than does any other method, for as yet the results of radium and X-ray treatment have proved to be very disappointing. The cervical oesophagus, although it is less often the site of carcinoma than the lower part, can be safely and completely removed in a considerable number of cases at a certain stage of involvement. The drawbacks are an advanced state of the pathological condition and the age, usually over sixty, and the presence of bronchitis, emphysema and cardiovascular degeneration. Since the feasibility of intrathoracic operation has been fully established, this route has usually been adopted as the approach for removal of the greater part of the oesophagus.

Dickes, R., Knudsen, A. F., and Franco, S. C. (1942) *Arch. intern. Med.*, 70, 121.

Turner, G. G. (1942) *Proc. Cardiff med. Soc.*, p. 5.

OVARY DISEASES

See also B.E.M.P., Vol. IX, p. 318; and Cumulative Supplement, Key Nos. 1191–1196.

Tumours

Aetiology and classification

Meigs's syndrome.—W. W. Herrick, T. L. Tyson and B. P. Watson report a case in a widow, aged seventy-five years, of Meigs's syndrome. The latter is applied to the association of hydrothorax with ovarian fibroma, of which J. V. Meigs in 1939 collected fifteen cases, the average age of the patients being fifty-one years. The first reported case was that described by C. J. Cullingworth, later of St. Thomas's Hospital, and as in the case reported by Herrick, Tyson and Watson, the patient had bilateral ovarian fibromas. The condition described by Herrick and his colleagues was first diagnosed as peritoneal tuberculosis, but subsequently this opinion was shaken in favour of a more serious view. A large fibroma of the right ovary and a small fibroma of the left ovary were removed. The laparotomy was followed by the spontaneous and permanent disappearance of the hydrothorax; this appears to be the usual course of events in all cases of Meigs's syndrome.

Clinical types

Gynandroblastoma.—W. C. Black records the case of a woman, aged twenty-four, with hirsuties, a masculine voice and beard, and hypertrophy of the clitoris, of five years' duration; menstruation, although varying in amount, had always been regular. Microscopically the ovarian tumour responsible for these signs was heterogeneous, with extensive necrosis. In parts the form and arrangement of the tumour cells corresponded with those of the sarcomatoid form of granulosa-celled tumour, but other parts consisted of impervious tubules with isolated cells, and groups of cells containing much lipin and resembling the interstitial cells of the testis. R. Meyer in 1930 gave this rare tumour its name of gynandroblastoma, a combination of a granulosa-celled tumour and an arrhenoblastoma, or a tumour of a hermaphrodite gonad. In Black's case, two and a half years after removal of the tumour in the medulla of the ovary, the woman's health was good, but the clitoris remained large and the other signs of masculinization persisted. W. Schiller referred to other examples of this rare tumour.

Thecoma of the ovary.—Josephine Barnes records with a historical summary a case of thecoma of the ovary, a comparatively rare solid primary tumour, always unilateral and so seldom malignant that unilateral oophorectomy may be the only treatment required. It was first described in 1927 by G. Moretti and P. Arrigoni under the title of 'fibroma thecozellulare xanthomatodes ovarii'. A more detailed account of six cases was given by E. Löffler and A. Priesel in 1934. Barnes collects twelve cases, one of which—that published in 1933 by J. H. Patterson and W. McK. H. McCullagh—was in Great Britain. The tumours are composed of epithelioid or connective tissue spindle cells, laden with fat droplets, mainly cholesterol and phospholipoids. E. Novak (1940) regarded the tumours as formed of granulosa cells which have undergone luteinization. Barnes's patient, aged forty-eight, had persistent uterine haemorrhage in spite of atrophy of the endometrium caused by radium. It is suggested that in all cases of ovarian fibroma, especially if there has been irregular uterine haemorrhage, a section of the tumour should be stained for fat; it is probable that these tumours are much commoner than is at present realized.

Treatment

In elderly women.—J. W. Goldsmith, Jun. in a paper read before the Brooklyn Gynecological Society considers the treatment of ovarian tumours in elderly women. He deprecates timidity in operating, but points out that patients over fifty years of age require special pre-operative care, rapid operation with minimal trauma and early activity after operation. The author advocates basal narcosis with local anaesthesia. Of eighty-six such cases, in fifty-one the tumour was malignant, in thirty-five benign. Of the group with malignant growths three patients died after the operation and 57.6 per cent were dead in five years. All the patients with benign tumours did well.

Barnes, Josephine (1943) *Proc. R. Soc. Med.*, **36**, 364.

Black, W. C. (1942) *Amer. J. Path.*, **18**, 766.

Goldsmith, J. W., Jun. (1943) *Amer. J. Obstet. Gynec.*, **45**, 518.

Herrick, W. W., Tyson, T. L., and Watson, B. P. (1943) *Arch. intern. Med.*, **71**, 370.

Meigs, J. V. (1939) *Ann. Surg.*, **110**, 731.

Meyer, R. (1930) *Beitr. path. Anat.*, **84**, 485.

Patterson, J. H., and McCullagh, W. McK. H. (1933) *J. Obstet. Gynaec.*, **43**, 1186.

Schiller, W. (1942) *Amer. J. Path.*, **18**, 766.

OZAENA

See also B.E.M.P., Vol. IX, p. 354.

Treatment

Medical methods

Oestrogens.—I. S. Hall and I. A. M. Macleod report twenty-three cases of patients with atrophic rhinitis who were treated by oestrogens; fifteen were females. Three preparations were used, in oily solution; one solution contained 10,000 international units per millilitre, the others contained 5 milligrams per cubic centimetre. After cleansing with a douche and, if

necessary, by mechanical removal of crusts, from $\frac{1}{4}$ to 1 cubic centimetre of oestrogen solution was sprayed into each nostril; the treatment was given daily. The average length of time required was six weeks in early cases and nine weeks in advanced cases. Ill effects were not observed. Symptomatic relief was obtained in all cases and apparent cure was produced in some. One elderly patient with chronic sinusitis did not respond any better than she did to simple douching; in the remaining cases the results were considered to be superior to those obtained by any other method.

Hall, I. S., and Macleod, I. A. M. (1942) *J. Laryng.*, **57**, 337.

PANCREAS, DISEASES

See also B.E.M.P., Vol. IX, p. 386; and Cumulative Supplement, Key Nos. 1203–1208.

Fistulae

The pancreatic secretion

Summary of tests made.—M. W. Comfort, A. E. Osterberg and J. T. Priestley report the following case. A man thirty-nine years old complained of the discomfort arising from an external pancreatic fistula dating from an operation three years before when a pancreatic cyst had been drained, and of attacks of severe upper abdominal pain associated with chills and vomiting. Physical examination was negative apart from the presence of the fistula, which opened just above the umbilicus. An indwelling catheter was inserted and left in position for a month. At the end of that time operation was performed. The fistulous tract was dissected out and transplanted into the anterior wall of the stomach. The gall-bladder, which contained stones, was removed. The patient was well five months later. During the period preceding operation, observations were made on the pancreatic secretion, with the following results. (1) When the gastric juice was excluded from the duodenum by continuous aspiration of the stomach the fasting secretion of pancreatic juice was mostly small in amount and low in bicarbonate and enzyme content. It was not measurably increased by introduction of glucose and casein through a tube into the duodenum, and only slightly increased by introduction of olive oil. (2) When the gastric juice had free access to the duodenum, secretion was generally scanty and low in bicarbonate content. (3) Gastric juice plus food powerfully stimulated secretion. Meals containing much fat evoked less secretion than did meals high in protein and carbohydrate. (4) Secretin administered intravenously appeared to equal or somewhat to exceed in potency the normal gastric mechanism. Mecholyl (acetyl- β -methylcholine chloride), while it had no effect alone, in combination with secretin evoked more abundant juice than did secretin alone. (5) Ephedrine and atropine diminished the amount of secretion and the total values for sodium bicarbonate and lipase but did not affect the total amylase values.

Cysts

Types of cyst

Fibrocystic disease.—W. A. Daniel, Jun. reports eight cases of fibrocystic disease of the pancreas—a rare familial disorder of early childhood which is characterized by malnutrition, chronic cough and the passage of large fatty stools. The above symptoms are associated with absence or with deficiency of pancreatic enzymes in the duodenal contents, the test for which is difficult to carry out in a young child and one which was not, in fact, performed in any of the author's cases. The pathological changes which were found at necropsy include bronchitis, broncho-pneumonia or multiple abscesses of the lungs, and fibrosis with cyst formation in the pancreas. Significant changes are not found in the intestines. The disease almost invariably ends fatally but, if it is recognized in time, treatment by pancreatic extracts holds out a measure of hope. All but one of the present series of patients died, the only patient who received treatment, a girl, aged nine and a half months when first seen, is still living at the age of twenty-two months.

Tumours

Carcinoma of pancreas

Success of surgical treatment.—G. Gordon-Taylor draws attention to the increasingly successful results attained by surgery in carcinoma of the pancreas. An early resort to laparotomy is urged in all cases of obstructive jaundice, since even if radical operation is impracticable a palliative anastomosis may relieve symptoms and prolong life. (1) Carcinoma of the head of the pancreas is the most common form. Pain is usually present, jaundice less constant. Rapid loss of weight is a notable feature. The dilated gall-bladder occurs in about 46 per cent of cases. Radiography may demonstrate deformity of the duodenum and the estimation of pancreatic ferments in the blood may assist diagnosis. In many cases the tumour arises in close relation to the termination of the common bile-duct; such growths, the so-called ampullary tumours, are of low malignancy, remain operable for a comparatively long time and have been successfully treated by limited local removal. Some of these growths have been found to respond to radium. (2) Cancer of the body of the pancreas is characterized by pain without jaundice. The pain tends to be worse when the patient is in the recumbent position, hence it generally occurs at night. A palpable tumour may be present. Radical removal may entail ligation and removal of the splenic vessels or removal of a lateral strip of the portal vein. (3) Cancer of the tail of the pancreas produces few symptoms and the clinical picture is

vague and ill-defined. Few cases therefore come to operation at a sufficiently early stage to allow of radical extirpation of the growth.

Comfort, M. W., Osterberg, A. E., and Priestley, J. T. (1943) *Amer. J. digest. Dis.*, **10**, 7.

Daniel, W. A., Jun. (1942) *Amer. J. Dis. Child.*, **64**, 33.

Gordon-Taylor, G. (1943) *Practitioner*, **150**, 257.

PARALYSIS AGITANS

See also B.E.M.P., Vol. IX, p. 408.

Treatment

Vitamin B complex

Winifred C. Loughlin, H. A. Myersburg and H. Wortis have treated a series of twelve patients who were suffering from paralysis agitans of long standing, by administration of the B vitamins. Each patient received six intravenous injections of vitamin B complex per week for ten and a half weeks, in addition to any other treatment that they had been having previously. A control group of ten patients received a similar course of intravenous injections of normal saline. No evidence was obtained that paralysis agitans is related to vitamin B deficiency. Two of the treated patients experienced some subjective improvement but so also did three of the control group. One of the latter even showed objective improvement, which was not observed in any of the treated patients.

Loughlin, Winifred C., Myersburg, H. A., and Wortis, H. (1942) *Ann. intern. Med.*, **17**, 423.

PARAPSORIASIS

See also B.E.M.P., Vol. IX, p. 419; and Cumulative Supplement, Key No. 1213.

Clinical picture

Clinical types

Histological changes.—H. Montgomery and R. J. Burkhart review fifty-two cases of parapsoriasis, classified as follows. (1) Parapsoriasis guttata (twenty-four cases). The histological changes include parakeratosis usually, slight or moderate acanthosis, elongation of the papillary bodies, intracellular and occasionally extracellular oedema, areas of degeneration of the basal cell layer and infiltration of the upper cutis. The disease persists, with remissions, for many years and occasionally disappears with or without treatment. (2) Parapsoriasis varioliformis (five cases). A variety of, sometimes reverting to, parapsoriasis guttata. The lesions are diverse in appearance, and the histological changes are those of acute inflammation; spontaneous involution is commoner in this than in the foregoing type. (3) Parapsoriasis *en plaques* (twenty cases). The histopathology resembles that of parapsoriasis guttata, but oedema of the cutis is more pronounced. (4) Parapsoriasis (parakeratosis) variegata (three cases). The authors differ from some authorities in considering this to be a genuine parapsoriasis. Dilatation of the capillaries and liquefaction of the basal cell layer are more pronounced than in parapsoriasis guttata. (5) Transitional forms were seen in many of the cases. The cause of parapsoriasis remains unknown. Types (3) and (4) in rare instances terminate in mycosis fungoides or other forms of lymphoblastoma, but are not a prodromal phase of the latter. No evidence of a tuberculous origin has been obtained.

Montgomery, H., and Burkhart, R. J. (1942) *Arch. Derm. Syph., N.Y.*, **46**, 673.

PARATHYROID GLAND DISEASES

See also B.E.M.P., Vol. IX, p. 424; and Cumulative Supplement, Key Nos. 1214–1216.

The parathyroid glands

Physiology

Parathyroid hormone action on bones.—H. Selye has conducted a series of experiments on rats with a view to testing the hypothesis that the action of the parathyroid hormone upon bone is an indirect one, mediated by the kidney. The effects of thyroidectomy and of partial hepatectomy were also investigated. Forty-eight rats were divided into four groups, each consisting of six males and six females. Group 1 was thyroidectomized, group 2 was bilaterally nephrectomized, group 3 was partially hepatectomized and group 4 was left intact as a control. Sixteen hours after the various operative procedures had been completed every animal received a subcutaneous injection of 20 units of parathyroid hormone. Twenty hours later the rats were killed, with the exception of six of the nephrectomized animals—three of each sex—which had already died. Metastatic calcification in the soft tissues was found scarcely to have begun, but absorption of bone was conspicuous even at this early stage. Calcium deposits were present in the lumina of the renal tubules. The changes were similar in all four groups and no evidence was obtained that the various operations in any way influenced the results. Other experiments confirmed previous work showing that slight osteoclastic changes, simulating those brought about by administration of parathyroid extract, occur after nephrectomy and can be prevented by parathyroidectomy. It is concluded that nephrectomy probably affects the bones by stimulating the production of parathyroid hormone.

The nature of tetany and the effect of adrenaline.—A. M. Harvey and J. L. Lilienthal, Jun. have followed up W. Falta's experiments showing the increased sensitivity to adrenaline of

people with low serum calcium values by injecting adrenaline into the brachial artery in five patients with tetany, one hypercalcaemic individual and three normal controls. In each case the patient was warmed before the injection was given, by means of blankets, electrically heated pads and immersion of one leg in hot water, until generalized vasodilatation was shown by flushing, sweating and rise of skin temperature. Heating was continued throughout the experiment. A sphygmomanometer cuff was used to obstruct the venous return from the injected arm for from one to two minutes and was then released. The following observations were made. (1) Normal subjects. A dose of from 0.15 to 0.6 gramme (2½ to 10 grains) of adrenaline produced immediate blanching and cyanosis of the limb, cessation of sweating, reduction of the radial pulse volume and prolonged decrease of skin temperature. When the sphygmomanometer cuff was released general symptoms occurred, including headache, tachycardia and facial pallor, and the skin temperature of the other extremities fell but returned to its former height within five minutes. (2) Patients (three) with tetany resulting from hypoparathyroidism and with serum calcium values of between 4.9 and 7.0 milligrams per cent. Injection of 0.3 gramme (5 grains) of adrenaline produced local and general reactions similar to but much more intense than those observed in the normal subjects and in addition tetany appeared in the hand of the injected side and on release of the cuff became generalized. (3) Patients (two) with tetany not of hypocalcaemic origin. The first was a young man who developed carpopedal spasm after two minutes of overbreathing. The second was a woman of thirty-two who had apparently suffered from genuine tetany ten years before after a subtotal thyroidectomy, and in whom symptoms developed afresh during a period of emotional stress. Both patients had normal serum calcium levels and both reacted to adrenaline as the normal controls did. (4) A patient with parathyroid adenoma and serum calcium of 17.1 milligrams per cent. The reactions were normal. The conversion of a latent into a manifest tetany by emotional strain or exercise may be brought about by the release of adrenaline during such periods. The action of adrenaline may be due to sudden disturbance of the calcium-potassium balance. The authors stress the dangers attending its administration to patients in whom the serum calcium level is low.

Falta, W., and Rudinger, C. (1909) *Verh. Kongr. inn. Med.*, **26**, 405.

Harvey, A. M., and Lilienthal, J. L., Jun. (1942) *Johns Hopk. Hosp. Bull.*, **71**, 163.

Selye, H. (1942) *Arch. Path.*, **34**, 625.

PAROTID GLAND DISEASES

See also B.E.M.P., Vol. IX, p. 449; and Cumulative Supplement, Key Nos. 1217–1226.

Acute parotitis

Aetiology

Surgical parotitis.—W. T. Coughlin and E. R. Gish group all acute inflammations of the parotid gland, except mumps, under the title of 'surgical parotiditis'. Infection may reach the parotid gland through the blood stream, through the lymphatic vessels, along the parotid duct or by direct extension. The authors' experience leads them to believe that infection through the duct is the most common cause and is favoured by absence of salivary flow, which enables bacteria to ascend the duct. Staphylococci are the most common causal organisms. The disease is less uncommon than has been supposed. among 95,367 admissions to the St. Louis hospitals, fifty-six cases of parotiditis occurred, of which forty-four began while the patient was in hospital, that is the condition complicated other diseases; this gives an incidence of 1 in 2,167 cases. The sex incidence showed a preponderance of females, males numbering only twenty-four. The youngest patient was nine years, the oldest eighty-seven; 57 per cent of the cases occurred in the third, fourth and fifth decades of life. Weather possibly exerts some influence; nearly one-third of the cases occurred in 1936, when the summer was the hottest ever recorded in St. Louis, and 45 per cent of the cases for that year were admitted during the three hottest months. The incidence for 1936 was 1 in 647 admissions. In 20 per cent of the patients, advanced renal arteriosclerosis was present. Five patients were diabetics. In twenty-five of the cases it was noted that the condition of the mouth was 'dry', 'dirty' or 'foul', or that caries or pyorrhoea was present. In seven of the cases the patient was not being fed by mouth, and the suggestion is made that in such cases the patient might advisably be given something to suck in order to maintain the flow of saliva. In only three cases was the condition associated with pneumonia, and in one case with a stone in the parotid duct. The onset was more often sudden than gradual, and the progress was rapid. The inflammation may subside without drainage, or it may burst spontaneously or drain through the duct. Extension into the neck is a frequent and serious complication; the mortality in such cases was 50 per cent, contrasted with a mean mortality of 34 per cent. Treatment consists in large doses of sulphonamide compounds, followed by early operation if the process does not subside. The procedure advised is to strip the capsule from the superficial surface of the gland and to make multiple incisions into the gland substance with unopened blunt scissors.

Coughlin, W. T., and Gish, E. R. (1942) *Arch. Surg., Chicago*, **45**, 361.

PEMPHIGUS AND PEMPHIGOIDS

See also B.E.M.P., Vol. IX, p. 482; and Cumulative Supplement, Key Nos. 1229–1233.

Definition*Other diseases accompanied by bullae*

Historical review and nomenclature.—A historical study of pemphigus by W. F. Lever and J. H. Talbott recalls that the word was first used by Hippocrates, who described a 'pemphigoid fever', but he left no clue concerning the disease he meant. Diseases associated with blisters are described in his writings but evidence cannot be found that pemphigus as a clinical entity was known to him. Celsus, Galen, Aetius and Rhazes all described diseases characterized by blisters, some of which may have been cases of pemphigus but this cannot be proved. There is not any description of a disease resembling pemphigus to be found in mediaeval European literature. The first unmistakable case of pemphigus in the literature is that recorded by S. Koenig, a Swiss physician, in 1681; in a woman, aged twenty-five, blisters the size of a hand developed on different parts of the body. When the blisters disappeared from one area they appeared in another. After eight months the patient was well enough to leave the hospital, and she remained well for nine months; then the blisters reappeared but persisted only for ten days. A second free interval of nine months was succeeded by a third reappearance of the blisters; after this no further recurrence took place. Koenig did not give any name to the disease. The word, pemphigus, was first used by de Sauvages in 1760 to describe a bullous eruption of short duration (probably erythema multiforme), and with this connotation it appears in the works of other authors. The only other description to be found in the literature, up to 1789, of what appears to be true pemphigus is given by an Irishman, D. Macbride in 1777, who, however, called it not pemphigus but 'morbus vesicularis'. In 1791 Wichmann gave to the word pemphigus its present meaning, that is a chronic bullous disease, not necessarily febrile; this definition was endorsed by Hebra who, in 1860, classified Wichmann's pemphigus as pemphigus vulgaris, the name by which it has been known ever since. Of the two other recognized forms, pemphigus foliaceus was described in 1844 by Cazenave and pemphigus vegetans in 1886 by Neumann. Three additional varieties described in recent years are not generally recognized as requiring separate classification; they are the malignant subacute pemphigus of Brocq, the chronic benign pemphigus of mucous membranes described by Thost and by Serefis, and the pemphigus erythematodes of Senechal and Usher, which combines the features of pemphigus with those of lupus erythematosus.

Lever, W. F., and Talbott, J. H. (1942) *Arch. Derm. Syph., N.Y.*, **46**, 800.

PEPTIC ULCER

See also B.E.M.P., Vol IX, p 504, and Cumulative Supplement, Key Nos. 1236 and 1237.

Peptic ulcer of stomach and duodenum*Aetiology*

Psychological factors in gastro-duodenal disturbances.—The relation between the emotions and gastro-duodenal function is discussed in a Leading Article in the *Lancet*. The significance of psychic factors in the genesis of peptic ulcers has long been recognized and attempts have been made in the United States of America to correlate emotional states with changes in gastric motility and secretion. Experiments were carried out upon normal people and upon patients with peptic ulcer who were made to swallow a thin rubber balloon attached to one of a pair of rubber tubes. The balloon was inflated in the stomach and connected through a water manometer to a kymograph by which the gastric contractions were recorded. Through the second tube gastric juice was withdrawn by continuous suction. Movements of the chest wall and variations of finger temperature were also recorded. Each subject was examined repeatedly under different conditions of mental repose or excitement. The mental stimuli applied were chosen to undermine the subject's sense of emotional security and to reinstate old stresses. It was found that tension, anxiety, resentment or anger was almost invariably accompanied by increase of secretion of hydrochloric acid and pepsin; peristalsis became continuous and the contractions more ample; respiration became more rapid and more shallow; and a drop in finger temperature usually occurred. Such changes were noted in both the normal and the ulcer subjects. In one patient with a gastrostomy visible dilatation of the gastric blood vessels also occurred, and it is inferred that changes in gastro-duodenal vascularity are a regular part of the emotional reaction. In a small minority of subjects emotional stimuli caused changes in the opposite, that is the inhibitory, direction. In such people fear appears to be the dominant feeling. Ulcer patients did not exhibit this type of response.

Role of the hypothalamus and autonomic system.—B. B. Crohn discusses the psychogenic aspect of peptic ulcer and speculates upon the mechanism involved. Recurrent psychic trauma may either initiate ulceration or maintain activity in an ulcer already formed. The hypothalamus dominates the functions of the autonomic system, thus controlling the secretion, motility and vasomotor activity of the alimentary canal. It is probably also a coordinating centre for the emotions. Stimulation, in animals, of the posterior part of the hypothalamus produces manifestations of anger. In human subjects psychic depression and loss of inhibitions are associated with tumours involving the hypothalamic region. The effect of recurrent emotional disturbances emanating from the cerebral cortex may act through the hypothalamus and the autonomic system upon the alimentary tract. In a case recently reported an acute duodenal ulcer caused death from bleeding in a youth of sixteen who had a severe crushing injury to the cervical spinal cord due to diving into shallow water seventeen days

previously. The mechanism involved may have been interruption of the sympathetic pathways in the cord and consequent unopposed action of the vagus system. Experimentally, peptic ulceration has been observed to occur after prolonged stimulation of the vagi, administration of acetylcholine, intravenous injections of pilocarpine and severance of the splanchnic nerves or removal of the coeliac plexus.

Diagnosis and differential diagnosis

Benign or malignant.—F. Steigmann from a study of more than 200 patients has reached the conclusion that no diagnostic criterion, clinical, radiological or gastroscopic, exists whereby the benign or malignant character of large gastric ulcers can be conclusively established and that resection is advisable in all such cases. In some instances only histological examination will settle the diagnosis. In all these patients a large ulcer, diagnosed after full investigation as benign, failed to show signs of healing after three to four weeks of intensive medical treatment and exploratory laparotomy was then carried out. In a large (unstated) proportion malignant disease was found.

Treatment

Treatment in the Forces.—H. J. Wade has studied 1,003 cases of dyspepsia seen at a Royal Naval Auxiliary hospital during the two years October, 1939 to October, 1941. During the first year of the present war many men with long histories of peptic ulceration were given treatment and then discharged to duty with advice as to diet. In March, 1941, however, it was decided to recommend for discharge any patient with proved active ulceration, and any patient with recurrence of symptoms without radiological proof but with a past history of gastro-duodenal operation, perforation or haematemesis. Exceptions were officers and specialist ratings who could be employed ashore under conditions of proper dietetic control. Patients complaining for the first time of dyspeptic symptoms are fully investigated and, if the findings are inconclusive, are returned to duty for a trial period. If they return to hospital they are then treated as ulcer cases, that is they are given shore duty or discharged. The author's series included sixty-seven gastric, 404 duodenal and five anastomotic ulcers. As compared with gastric ulcer the duodenal ulcer cases showed an earlier age of onset, earlier development of complications, greater influence of psychological factors and greater frequency of a family history of ulceration. Many of the patients with peptic ulceration were new entrants who had suffered from the complaint in civil life and relapsed after a short period of active service. Evidence was not obtained that war service has increased the incidence in the Royal Navy either of peptic ulceration or of dyspepsia as a whole. Dyspepsia accounted for about 9 per cent of all admissions in each quarter of the years under consideration, and peptic ulcer for about 55 per cent of the dyspepsia cases.

Inefficacy of vitamin A.—A. H. Douthwaite has tested and failed to obtain much support for the claims made for vitamin A in the treatment of chronic gastric ulcer, by administering it to twelve patients who, while under treatment, were told to eat ordinary food and not to take extra rest. In all cases the diagnosis was confirmed by X-ray examination and by the finding of occult blood in the stools. The first eight patients received 120,000 units daily for three weeks. All grew worse and in one man who was X-rayed at the end of the course the size of the ulcer had not diminished. All subsequently responded well to orthodox medical treatment. The ninth patient, who was allowed to smoke as much as he liked whilst under treatment, received the same dosage for a fortnight, by which time pain had ceased and ulceration was not visible in the X-ray film. Three patients who received larger doses (240,000 units daily) for four weeks did not experience any benefit.

Operative results at the Mayo Clinic.—The results of operations on the stomach and duodenum performed at the Mayo Clinic during 1941 are reported by W. Walters, H. K. Gray, J. T. Priestley and V. S. Counseller. The number of operations was 1,000, of patients operated on 991. The mortality rate was 4.3 per cent. Of the total number of patients attending for duodenal ulcer, 435 (18 per cent) were operated on. In 215 cases resections were performed, with a mortality of 2.8 per cent. Gastro-enterostomy was carried out in 198 cases, with a mortality of 1.5 per cent. Operation was performed only in cases in which complications had arisen or when prolonged medical treatment had failed. For gastric ulcer ninety-seven patients underwent operation. Partial gastrectomy was done in eighty-eight cases, with a mortality rate of 1.1 per cent. Twenty-seven patients had both gastric and duodenal ulcers, and underwent partial gastrectomy without fatality. The advisability of operation in cases of chronic gastric ulcer is strongly urged, in view of the comparative safety of partial gastrectomy, the inefficacy of medical treatment and the danger of a cancer being missed. Forty patients with anastomotic ulcer were treated by partial gastrectomy, with a mortality of 7.5 per cent. For various other benign lesions partial gastrectomy was performed in forty-eight cases. The total mortality for partial gastrectomy for non-malignant lesions was 2.6 per cent. In 105 cases of cancer the mortality for partial gastrectomy was 13.3. Total gastrectomy was done in eight cases, with four deaths. Twenty-nine other cases of cancer were treated by palliative gastro-enterostomy, with a mortality of 6.9 per cent; and 122 explorations were carried out with a mortality rate of 3.3 per cent. Exploration is now advised in all cases of cancer free from evidence of distant metastasis, and the number of resections has risen in almost direct proportion to the increased number of laparotomies.

After perforation.—C. Harrison and F. W. Cooper, Jun. have studied a series of fifty-seven cases in order to test the validity of the theory that perforation of a peptic ulcer is followed—

if the patient recovers—by permanent healing. The group consisted of fifty duodenal and six gastric perforations, and the operative procedure in all was simple closure of the hole and cleaning of the peritoneal cavity. The average age of the patients was forty-one years, and the average duration of symptoms prior to perforation was 6·3 years. Correlation was not to be found between either the size of the perforation or the lapse of time before operation and the amount of fluid in the peritoneal cavity, nor between the size of the perforation and the presence of free gas. The mortality rose abruptly in cases in which the ulcer had perforated more than ten hours before operation; when perforation had occurred less than ten hours before, the mortality was 13·3 per cent; between ten and twenty hours, 41·6 per cent; over twenty hours, 46·6 per cent. All the patients (forty-one) who recovered were kept subsequently under constant supervision, and it was found that symptoms had recurred in 82·5 per cent. One patient had a second perforation. It is concluded that treatment is no less necessary for a patient who has survived a perforation than in any other case of peptic ulceration.

Crohn, B. B. (1942) *Amer. J. digest. Dis.*, **9**, 358.

Douthwaite, A. H. (1942) *Guy's Hosp. Rep.*, **91**, 97.

Harrison, C., and Cooper, F. W., Jun. (1942) *Ann. Surg.*, **116**, 194.

Leading Article (1942) *Lancet*, **2**, 548.

Steigmann, F. (1943) *Amer. J. digest. Dis.*, **10**, 88.

Wade, H. J. (1942) *Lancet*, **2**, 636.

Walters, W., Gray, H. K., Priestley, J. T., and Counseller, V. S. (1942) *Proc. Mayo Clin.*, **17**, 420.

PERITONITIS: ACUTE PERITONITIS

See also B.E.M.P., Vol. IX, p. 537; and Cumulative Supplement, Key No. 1241.

Treatment

Prophylactic

Peritoneal immunity.—H. B. Morton has studied the cytological reaction associated with the development of peritonitis or peritoneal immunity. Earlier experiments showed that an immune reaction can be induced by various substances introduced into the peritoneal cavity and that this reaction consists of the appearance of numerous macrophage cells. It was inferred that these cells were derived from the omentum, a view confirmed by the present study, in which biopsies were made of omental tissue taken from patients who had some acute abdominal inflammatory disease or who had received intraperitoneal injections of amniotic fluid concentrate before undergoing an operation upon the colon. Microscopical sections showed dilatation and engorgement of the capillaries and cellular infiltration of the surrounding tissue, the cells consisting of polymorphonuclear leucocytes and monocytes in varying proportions. The longer the duration of the irritation, the more do monocytes, that is macrophages, preponderate. They seem to originate in the perivascular region, possibly from the capillary endothelium, and they appear in the omentum before they can be found in the peritoneal fluid. Development of peritoneal immunity is thus a process requiring time. Deliberate pre-operative immunization is therefore seldom possible, but in emergency work the use of sulphathiazole, for example, may encourage the development of immunity ahead of the spread of infection.

Morton, H. B. (1942) *Surg. Gynec. Obstet.*, **75**, 202.

PHARMACOLOGY

Antiseptics

Historical survey

An interesting account of the changes of scientific opinion on the scope of antiseptics and its practice has been given by L. P. Garrod who speaks with much practical experience. There have been three eras of thought and practice in this connexion. The first of these periods extends from the pioneer work of Ignaz Philipp Semmelweis (1818–65) and Joseph Lister (1827–1912), the second to the later part of the war of 1914–18, and the third dates only from 1940. From the seventh decade of the last century, when 'pus ceased to be laudable and laparotomy to be homicidal', the great revolution in surgery was in large part due to simple cleanliness and the introduction of methods now called aseptic. Whatever the share of antiseptics in first making surgery safe, carbolic acid is a very bad one by modern standards, and it was upon this that Lister relied. His use, and that of cresols in various forms which are almost equally caustic and destructive of tissues, continued for many years. Other antiseptics employed in early days included mercury salts which damage exposed tissue and are inactivated by blood protein and boric acid and are too weak for action on bacteria. The early failure was followed by the era of septicism, lasting throughout the inter-war period. During this time most surgeons when asked if they believe an antiseptic can disinfect a wound say 'no', and the orthodox creed was to the effect that antiseptics do more harm to the tissues than do bacteria. This conclusion was not true of the flavines, and their merits have been for more than ten years proclaimed before an unheeding world. The third period, that of rehabilitation of antiseptics as a method of wound treatment has followed the discovery that the sulphonamides act locally. The importance of A. Fleming's discovery of the antibacterial power of penicillin,

has been more recently followed up by Professor H. W. Florey at Oxford. A generous tribute is paid to the work of D. D. Woods and P. Fildes's work on bacterial chemistry which has played such an important part in the recent development during the last two or three years of the local treatment of wounds.

Cardiac tonics

Ouabain

Thirty-seven patients with rapid cardiac arrhythmias have been treated with ouabain by W. I. Geffer and W. G. Leaman, Jun. The series included two cases of paroxysmal auricular tachycardia, four of auricular flutter, twenty-four of auricular fibrillation, two of simple tachycardia and one of paroxysmal ventricular tachycardia. Four additional patients, all extremely ill, are excluded because they died shortly after injection of ouabain. Each patient received 0.5 milligram intravenously, and then an hour later a large oral dose (4 to 8 cat units) of digitalis leaf. Further doses of digitalis, 1 cat unit daily, were begun twenty-four hours after the initial treatment. Ouabain was found to be a valuable aid to full digitalization, producing a significant reduction in ventricular rate in twenty-eight of the thirty-three patients. The best results were obtained in congestive heart failure associated with rheumatic heart disease. The drug is comparatively ineffective in simple tachycardia and in the presence of severe infections. Toxic effects were rare: vomiting occurred in two cases and electrocardiographic abnormalities were observed in three (inversion of T wave in one case, coupled ventricular extrasystoles in two cases). It was impossible to decide whether the four deaths were caused or hastened by the drug.

Cetyl trimethyl ammonium bromide (C.T.A.B.)

Uses in surgery

Limitations in effect—R. Williams, Barbara Clayton-Cooper, J. McK. Duncan and Ellen M. Miles record a number of investigations on the possibilities of cetyl trimethyl ammonium bromide (C.T.A.B.) in surgery. Its disinfectant powers, tested *in vitro* against various organisms, were so decidedly reduced by the presence of organic matter that from that point of view it is ineffective. It proved, however, to be an excellent material for cleansing the skin, accidental wounds and the surgeon's hands, far exceeding soap and water in efficiency. The drawbacks are that it removes the natural oils from the skin and is apt to cause skin reactions in sensitive people.

Chemotherapy

The fight against virus disease

C. H. Andrewes, H. King and M. van den Ende in a short paper set out the results of very important and extensive work. Claims to chemotherapeutic success against a number of virus infections have failed to be substantiated. The only reproducible results have been against the relatively large viruses in the group containing lymphogranuloma venereum and trachoma viruses. The most extensive work has been carried out on the action of the sulphonamides on the first of these viruses. The extensive experimental trials made in connexion with the viruses of influenza A, lymphogranuloma venereum and vaccinia were essentially negative: not one of the 115 chemical substances of various kinds exerted any beneficial influence on influenza A virus of mice; tests of forty drugs against the virus of lymphogranuloma venereum in mice did not exert any beneficial effect, apart from that of the sulphonamide group, and the power of seventy-four compounds to inactivate vaccinia virus *in vitro* did not do so in such dilutions as would give promise of chemotherapeutic value.

δ -desoxyephedrine hydrochloride

A. C. Ivy and F. R. Goetzl review the literature relating to δ -desoxyephedrine hydrochloride (pervitin). The action of this drug on human beings and on animals resembles that of amphetamine sulphate but is more powerful. In from 3-milligram to 6-milligram doses it appears to produce psychological exaltation without undesirable side-effects, and the drug is said to be in use in the German armed forces for this purpose. Other effects of δ -desoxyephedrine hydrochloride are to reduce sensitivity to pain and to counteract the depressing effects of morphine without affecting its analgesic properties. Hypertension, cardiac disease, advanced age, thyrotoxicosis and insomnia are diseases usually regarded as conditions in which the drug is contra-indicated. Sleep may be disturbed at night when δ -desoxyephedrine hydrochloride has been taken during the day, and sedatives may then be required. German authors state that it is not a habit-forming drug, but it is admitted that certain persons become unable to stay awake without it. Tolerance is also observed.

Demerol

Effects in spasmodic cases

R. C. Batterman and J. H. Mulholland have made a clinical trial of demerol as a substitute for morphine and its derivatives in the control of post-operative pain, and give a favourable report. Demerol (1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester) possesses both sedative and anti-spasmodic properties which should make it a valuable drug for pain of a colicky character. It may safely be used, except in rare cases of hypersensitivity, to treat patients with severe anaemia, disease of the liver or kidneys or bronchial asthma. Respiratory depression very rarely occurs in connexion with demerol. In the present series of 488 post-operative patients, 165 had had abdominal section and of these 164 received the drug parenterally with complete relief of pain and discomfort in 95.5 per cent. After procedures other than laparo-

tomy demerol proved almost equally satisfactory, complete relief being obtained in 91·5 per cent of cases and moderate or transient relief in a further 5·2 per cent. The amount given varied between 50 and 150 milligrams in a single dose or repeated doses. With rare exceptions, whatever the surgical procedure had been, the administration of 75 to 100 milligrams of demerol parenterally every three or four hours sufficed to keep the patient comfortable. Orally the drug proved effective when pain was not severe, or after the initial post-operative symptoms had subsided. In 118 patients to whom it was given, 87 per cent of the results were successful. Toxic effects (dizziness and nausea) were rarely observed and no case of respiratory depression occurred.

The diamidine compounds

Propamidine

In wounds and burns.—The antiseptic action of propamidine, one of the diamidine compounds, has been the subject of intensive study, and the results are discussed in a Leading Article in the *Lancet*. Propamidine, 0·1 per cent, in a jelly or cetyl alcohol preparation, is applied to the wound or burn on alternate days for ten days. This treatment frees the wound from streptococci and often, although not always, from staphylococci; it has little action on *B. proteus* or *B. pyocyanus*. In the above concentration propamidine does not injure granulation tissue nor does it adversely affect phagocytosis; higher concentrations may cause local necrosis and irritation of the skin edges. Its antibacterial action is not inhibited by pus or by *p*-aminobenzoic acid and is not related to sulphonamide resistance. The drug when applied as described appears to give good results, either in infected wounds or in fresh burns. Animal experiments have provided evidence that propamidine is unlikely to control infection when given systemically by intravenous injection, and toxic manifestations, both immediate and late, have occurred after it has been administered. With local applications general toxic effects have not been observed but the possibility should be borne in mind when large lesions are present. The rate and the extent of absorption from raw surfaces are unknown.

Dicoumarin

Effect on prothrombin

For years it has been known that spoiled sweet clover has produced haemorrhagic disease in cattle, and recent researches have culminated in the isolation of an active principle, dicoumarin, which reduces the prothrombin content of the blood with consequent delay in clotting. E. V. Allen, N. W. Barker and J. M. Waugh have administered dicoumarin by mouth to 374 patients as a prophylactic against post-operative thrombosis and embolism. It produced considerable prolongation of the prothrombin time, persisting for days. Bleeding time was unaffected. The erythrocyte sedimentation rate was generally increased and clot retraction was retarded. When the drug was given as above a latent period of from twenty-four to forty-eight hours elapsed before its action was discernible. Dicoumarin had no effect when added to shed blood *in vitro*, showing that some factor in the body is necessary to enable it to act. It can be given intravenously but a stable preparation for this purpose is not yet available. Dicoumarin should be given only when frequent estimations of the prothrombin time can be made, because overdoses may cause serious bleeding. In the present series of cases the prothrombin time was measured daily, but the authors consider that the intervals may be increased safely to two or three days. The drug was administered in capsules containing 100 milligrams ($1\frac{1}{2}$ grains), of which two or three were given in one dose on the first day and two on the second day. On subsequent days the dose depended upon the prothrombin time, the aim being to maintain the level at between thirty-five and sixty seconds; if the prothrombin time was below this, 200 milligrams (3 grains) were given; if it was above, the daily dose was omitted. This regime was continued for as long as was considered necessary; after it was stopped the clotting time remained prolonged for a considerable time, gradually returning to normal. The responses of the patients varied, possibly owing to irregularities of absorption. Dicoumarin may be combined with heparin by giving the latter intravenously during the latent period before the former comes into action. The incidence of thrombosis and embolism among the treated patients was considerably reduced in comparison with the computed probable incidence. I. S. Wright and A. Prandoni have observed that a single dose of 600 milligrams (10 grains) was both less effective and less likely to produce toxic haemorrhagic manifestations than 100-milligram doses given daily. J. L. Bollman and F. W. Preston also stress the importance of continued administration. The effect of dicoumarin in dogs was greatly increased by vitamin K deficiency, by inanition or by damage to the liver or kidneys. W. L. Butsch and J. D. Stewart have used the drug with good results in cases of thrombosis and embolism. They emphasize the necessity for caution in cases with ulcerative or granulating lesions, from which severe or fatal bleeding is liable to occur.

Fluid administration

Clinical picture

Effects of overloading by fluids.—To determine the effects of overloading the circulation with fluid, E. P. Sharpey-Schafer and J. Wallace have made observations on a number of convalescent subjects without cardiovascular disease. (1) *Saline*. Nine subjects of ages varying from sixteen to fifty-six years were given quantities of from 300 to 2,000 cubic centimetres at rates of from 20 to 168 cubic centimetres per minute. (2) *Serum*. Eight subjects, aged seventeen to fifty-nine, received quantities of 700 to 2,100 cubic centimetres at rates of 54 to 154 cubic

centimetres per minute; five others, aged twenty-one to fifty-nine, each received 300 cubic centimetres of concentrated serum at rates of from 21 to 30 cubic centimetres per minute. (3) *Blood*. Two subjects, one aged forty and the other sixty-one years, received respectively 1,500 and 1,080 cubic centimetres per minute. The venous pressure rose in direct proportion to the retention of fluid in the circulation, as indicated by the haemoglobin concentration. Of fifteen patients, six showed a rise of pulse rate. Vital capacity was diminished in six out of seven cases. When the blood volume was first reduced by venesection, little rise of venous pressure occurred. Radiography showed increased diastolic size of the heart and, of twelve subjects, four showed slight electrocardiographic changes indicative of acute heart stress. Vasodilatation during the injection was noticed in all the subjects who showed retention of fluid in the circulation. Symptoms occurred in twelve patients (headache in eight, and a feeling of constriction in four).

Intravenous therapy

Mercurial diuretics

Investigation of fatalities.—H. Evans and K. M. A. Perry, reporting six cases of immediate death after an intravenous injection of a mercurial diuretic, point out that the cause of such deaths remains obscure. The suggestion that it is an acquired sensitivity to the drug receives support from the fact that in this series none of the deaths took place after the first dose. Four out of the six patients, and eight out of fifteen reported elsewhere, had nephritis type 2. Since many more patients with heart disease than patients with nephritis are receiving this treatment the preponderance of the nephritis group may be significant, and is possibly related to lowering of the plasma proteins or to a disturbed albumin-globulin ratio. The authors suggest that low plasma protein may be an indication for the use of the intramuscular route. The patients in the present series included the following. (1) A lad of seventeen with nephritis; he received a dose of 2 cubic centimetres of salyrgan (mersaly) without effect, so was given a second dose of 4 cubic centimetres and died immediately. (2) A woman of fifty-one, nephritis type 2, she died after her fourth injection of 2 cubic centimetres of salyrgan. (3) A man of fifty-one with rheumatic carditis and heart failure, he died after receiving half of his sixth injection of mersaly 2 cubic centimetres diluted to 10 cubic centimetres with normal saline. (4) A woman of forty-seven with nephritis type 2; she died during her third injection of salyrgan 1 cubic centimetre. (5) A man aged fifty-seven with arteriosclerosis and heart failure; he was treated with neptal 2 cubic centimetres twice weekly and died after the third dose. (6) A boy of seven with nephritis type 2; he received two injections of neptal, 1 cubic centimetre and 2 cubic centimetres respectively, four months intervening between the two injections. He died after the second injection. All the patients received ammonium chloride prior to having the injections.

Morphine

Cholinergic action on the stomach

Experimental observations.—D. Slaughter, A. B. Goddard and W. M. Henderson find that morphine acts on the stomach like a cholinergic drug. Observations made on five gastro-stomized dogs gave the following results. In appropriate doses morphine sulphate injected subcutaneously inhibits gastric tonus and contractions. Neostigmine (prostigmine methylsulphate), a known parasympathetic stimulant, produces a similar effect. If a subliminal dose of morphine is given either in combination with or shortly after a subliminal dose of neostigmine, inhibition develops. When the morphine has been given after the neostigmine the above effect is succeeded by a phase of increased activity; this rebound was not observed either with morphine in active doses or when the subliminal doses of morphine and neostigmine were given together, but sometimes it occurred after administration of an active dose of neostigmine. The authors seek to explain the above paradoxical action of a known cholinergic drug on the stomach by the presence in the vagus nerve of fibres with an adrenergic action; they cannot explain the rebound phenomenon.

Naphthalene compounds

Polar and non-polar compounds

Rate of corneal penetration.—Factors which affect the passage of drugs into the cornea have been studied by K. C. Swan and N. G. White. A series of experiments was designed to determine the comparative rates of penetration into the cornea by polar and non-polar substances, represented by various amino and sulphonic acid compounds of naphthalene. The test solution was allowed to flow over the cornea for three minutes; the excess was then washed off, the cornea was excised and weighed and the drug contained in it was extracted with dilute alcohol and estimated. It was found that with each addition of a polar group the rate of penetration was reduced. That such a reduction was not the result of increasing molecular weight was shown by substituting the phenyl for the naphthalene nucleus; the rate of penetration was not thereby increased. The only physical property which could be correlated with penetrating power was solubility in water and in lipoids. Naphthylamines, which are readily soluble in fats and are only slightly soluble in water, penetrated more rapidly than did the sulphonic acid compounds which are soluble in water and practically insoluble in fats. The affinity of the drug for the vehicle was found to influence the rate of penetration; polar compounds in water and non-polar compounds in oil tend to be retained in their vehicle and to enter the cornea slowly. This experiment was imitated *in vitro* by adding the compound

to be tested to a mixture of oil and water; it was found to become unequally distributed in proportion to its relative solubility in the two immiscible solvents. In another series of experiments the corneal epithelium was removed before the drug was applied and the results showed that penetration of non-polar compounds into the stroma was less rapid than into the epithelium and that of polar compounds much more rapid; in short, the difference in relative permeability for polar and non-polar compounds was greater in the epithelium than in the stroma. Thus the corneal epithelium does not act as a simple barrier; some substances penetrate more readily when it is intact. The influence of surface activity was studied with the aid of three local anaesthetics, pontocaine hydrochloride (butethanol), butyn and procaine hydrochloride, and it was found that the rate of penetration was directly proportional to the power possessed by the drug of lowering surface tension. Further experiments with procaine showed that the penetrating power increased with increasing pH of the vehicle; that moderate variations in osmotic pressure had not any effect, that penetration rate did not increase proportionately with increase in the concentration of the solution but rose significantly with the addition of a surface tension reducing agent; and that it was unaffected by variations in intra-ocular pressure except when such pressures were sufficient to cause damage to the epithelium.

Nicotine

Urinary excretion

Experimental assay of nicotine excretion. H. B. Haag and P. S. Larson have determined the nicotine excretion in the urine of four smokers by a modified silicotungstic acid method. Each subject smoked forty cigarettes a day; the daily elimination varied from 2.2 to 7.6 milligrams. To determine the influence of the urinary pH two series of experiments were conducted, in one the urine was kept acid by giving ammonium chloride, in the other alkalinity was maintained by citrates. The amount eliminated when the urine was alkaline was only 25 per cent of that noted when the urine was acid, presumably because nicotine is reabsorbed from the urinary tract when the urine is alkaline; this has been shown to occur in the cat. At most 15 per cent of the nicotine calculated to be derived from the tobacco smoke was excreted in the urine. In a further study the fate of the retained fraction was investigated. Dogs were given subcutaneous injections of 0.2 milligram of nicotine per kilogram of body weight (P. S. Larson and H. B. Haag). About 10 per cent was excreted unchanged in the urine. The remainder appeared in the urine, at least in part, as an unidentified component of the nicotinic acid fraction. This substance yields a rose colour in the presence of cyanogen bromide, on the addition of metol the colour changes to one which absorbs at the wave length of the nicotinic acid colour. Nicotine itself yields a greenish tint with cyanogen bromide. The rose colour fails to develop if the urine has previously been boiled.

Pancreatic extracts

A new pancreatic extract

L. W. Gorham and D. R. Climenko report the results obtained in the treatment of peripheral arterial disease by a new pancreatic extract. As long ago as 1928 an active substance was demonstrated in normal pancreatic tissue which when administered intravenously to animals produced a transient fall of blood pressure, increase of cardiac rate and increase of stroke volume. The active principle is not histamine, choline or peptone and is probably not related to adenosine since the authors have administered large doses of their preparation to dogs without producing heart block. This extract contains approximately 15,000 units of active substance per gramme, and lyophilized preparations retain their potency for at least two hundred and seventy days. It is prepared as follows. Finely ground pigs' pancreas, fresh or frozen, is suspended in water, the pH of the suspension is adjusted to 8.0, toluene is added as a preservative and the mixture is digested with trypsin at 37°C. Tryptic digestion destroys all insulin in the suspension. The mixture is then acidified with trichloroacetic acid and ammonium sulphate is added to one-third of saturation. The insoluble matter is centrifuged off. The supernatant liquid is then saturated with ammonium sulphate and the precipitate is centrifuged off and retained. It is dialyzed under toluene in Cellophane tubes against distilled water until it is free of sulphate, this process also removes any histamine or choline present. Water is finally removed by the Niphanoid process of drying under a high vacuum. The extract is standardized by biological assay, a unit being fixed as that quantity which when injected intravenously into an atropinized dog under sodium barbital anaesthesia will exactly counteract the effect of a minimal hypertensive dose of adrenalin. Experimentally in dogs intravenous administration of from 2 to 4 units was found to produce a considerable increase of limb volume, persisting long after the blood pressure, which at first falls sharply, has returned to normal. Intramuscularly the drug produced a similar increase of limb volume without affecting the blood pressure. In normal human controls intramuscular administration of 10 units was followed, after an initial decrease in some, by a considerable increase of limb volume, the increase being associated with a rise of skin temperature; and the response to cold was greatly reduced in intensity and duration, or abolished. Twenty-one patients were treated by injections of 10 units every two to seven days and in nineteen increased volume and symptomatic relief followed.

Penicillin

Effects in different cases

W. E. Herrell relates further encouraging experiences with penicillin at the Mayo Clinic.

Because of the limited amounts available penicillin should at present be reserved for severe infections with *Staphylococcus aureus*, *Streptococcus pyogenes* and susceptible strains of *Diplococcus pneumoniae*, *Neisseria gonorrhoeae* and *Neisseria intracellularis*, against all of which its efficacy has been experimentally proved. The best method of administration is by continuous or nearly continuous intravenous infusion of the pyrogen-free preparation. By this method the concentration of penicillin in the blood is maintained at a constant level and the danger of encouraging the development of penicillin-resistant organisms is minimized. The dosage advised is 30,000 to 40,000 Oxford units per twenty-four hours. Half of the dose is dissolved in a litre of normal saline or glucose solution (5 per cent in triple distilled water). The first 100 or 200 cubic centimetres is given fairly rapidly and the drip is then adjusted to deliver 30 to 40 drops per minute. The solution should be made up immediately before use. The drip is allowed to go on delivering glucose solution in the intervals of penicillin administration, so as to avoid the necessity for repeated venepuncture. When pyrogen-free penicillin has been used toxic reactions have not been observed. The following six cases were successfully treated in this way. (1) Facial and orbital cellulitis due to *Staphylococcus aureus*: blood cultures were positive; the patient received 160,000 Oxford units of penicillin in nine days. (2) Facial cellulitis with positive blood cultures due to *S. aureus*: the patient received 196,000 units in twelve days. (3) Acute pyelonephritis due to *S. aureus*: blood cultures were negative; the patient received 200,000 units in seven days. (4) Cellulitis of mouth and tongue due to a non-haemolytic streptococcus: blood cultures were negative; the patient received 64,000 units in four days. (5) Post-operative wound infection due to *S. aureus* with negative blood cultures: 88,000 units were given in five days. (6) Facial and nasal cellulitis due to *S. aureus* with negative blood culture: 132,000 units were given in six days. A patient with subacute bacterial endocarditis in which *Streptococcus viridans* was isolated from the blood did not show any improvement after receiving 128,000 units; blood cultures were still positive. Two cases of chronic ulcer due to *Staphylococcus aureus* were treated by local application of 2,100 units each, with good results. In one case of multiple abscesses and positive blood cultures due to *S. aureus* the patient recovered after receiving 4,200 units subcutaneously.

Effect on Staphylococcus aureus

Natural and acquired resistance to the drug.—In studying the effects of penicillin in infections in human beings, C. H. Rammelkamp and Thelma Maxon noticed that a favourable response was not always obtained in infections caused by *Staphylococcus aureus*. Further investigations were undertaken to determine what factors were involved in the resistance of this organism to penicillin. Strains of staphylococci used were all isolated from patients with clinical infections and were kept on blood agar slants until they were needed. The sensitivity of the organisms to penicillin was thus determined: serial dilutions of the sodium salt of penicillin were made, and a measured quantity of each solution was mixed with a measured quantity of a standard suspension of the culture to be tested. In this way the lowest concentration of penicillin required to kill twenty-nine strains of *S. aureus* was determined. It was found that different strains varied little in sensitivity: twenty-five out of the twenty-nine were killed by concentrations of penicillin of 0.04 to 0.08 Florey (Oxford) unit per cubic centimetre. By growing the organism to be tested in gradually increasing concentrations of penicillin it was shown that a considerable degree of resistance is acquired, for example the strain, aurice, showed a sixty-four-fold increase of resistance after fifty-four days' exposure. No correlation could be made out between the resistance of the organism and the clinical and bacteriological response to penicillin therapy. In fourteen cases observations were made on strains of staphylococci isolated from patients during a course of penicillin treatment. In only four cases was a change in the susceptibility of the organism demonstrated. In one of these cases resistance increased sixty-four-fold in eighteen days, in another sixteen-fold in two days. The nature of the acquired resistance of the staphylococcus is not known. No penicillin-destroying enzyme could be discovered in the resistant strains.

Toxicity and efficacy

Experiments on mice.—The pharmacological properties of penicillin have been studied by H. J. Robinson in mice. The material mostly used was penicillin (Merck) equivalent to 60 Florey units per milligram of solid. In a few experiments a more highly purified penicillin equivalent to 300 and 400 Florey units per milligram was employed. Solutions were freshly prepared in distilled water. (1) Toxicity determinations were made by injecting a 10 per cent aqueous solution intravenously or subcutaneously. Intravenously, the solution was given in single doses equivalent to 30, 60, 90 and 120 thousand Florey units per kilogram of body weight to a series of animals. The rate of administration was 0.1 cubic centimetre per minute. Subcutaneously, penicillin was administered three-hourly for five days, the daily dose ranging from 48,000 to 192,000 units. Intravenous administration of penicillin in the doses stated above was followed in all cases by signs of poisoning. The percentages of mice which died were: after 30,000 units, 0; after 60,000 units, 60; after 90,000 units, 90; after 120,000 units, 100. Subcutaneously, toxicity was much less severe. No mice died until a dosage of 192,000 units was reached and the percentage then was only 4. The more highly purified preparations appeared to be somewhat less toxic, weight for weight, than the preparation ordinarily used. (2) Efficacy was estimated *in vitro* against various micro-organisms by the 'rotating rock' technique, defibrinated blood being the test medium. Penicillin in dilutions of 1 in 2,000,000 was found to be rapidly bactericidal to *Streptococcus haemolyticus*, *Staphylococcus aureus* and

Diplococcus pneumoniae appeared to be somewhat more resistant and *Streptococcus viridans* much more resistant, requiring a concentration of 1 in 50,000. In experiments with cultures made on blood agar mixed with penicillin, inhibition of growth was observed for all Gram positive strains except *Streptococcus viridans*, *S. lactis* and one strain of *Staphylococcus aureus* at a penicillin concentration of 1 in 1,000,000. Most Gram negative strains were inhibited only at concentrations of 1 in 1,000. Considerable differences of resistance were observed among both groups of organisms. The bacteriostatic effect on anaerobic bacteria in a special medium was tested. Penicillin was found to be highly effective against *Clostridium welchii*, *C. tetani*, *C. botulinum* and *C. chauvoii*. *In vivo* experiments showed that subcutaneous injection of penicillin immediately after inoculation and at three-hourly or six-hourly intervals for five days afterwards protected mice against the Gram positive organisms. The total dose given was about one sixty-fourth of the previously determined toxic dose of penicillin when given by subcutaneous injection. Weight for weight penicillin appeared to be more effective than the sulphonamides in these infections. In experimental infections caused by the tubercle bacillus, *Trypanosoma equiperdum* and the influenza virus PR8 penicillin had not any apparent effect.

Uses in septic conditions

Various forms of administration.— M. E. Florey and H. W. Florey report the results of general and local administration of penicillin in cases of sepsis. Fourteen patients received penicillin by mouth or duodenal tube or by injection, 172 by local application; in one case general and local treatment were given. The advantages of local application are that smaller amounts of penicillin are required and the limited supplies available suffice for a larger number of patients. Of the fifteen serious cases in the first group ten were due to a staphylococcus, one (meningitis) to a sulphonamide-resistant streptococcus, three to actinomyces or streptothrix plus an anaerobic streptococcus and one (subacute bacterial endocarditis) to *Streptococcus viridans*. The staphylococcal cases included orbital cellulitis, osteomyelitis, cavernous sinus thrombosis and pyaemia or septicaemia. All the patients in this group recovered, as did the patient with streptococcal meningitis. Relapse followed in one patient who finally recovered under treatment with sulphathiazole. He received a total of 480,000 units of penicillin in enteric capsules and by duodenal tube. In the three cases of actinomyces or streptothrix infection the patients failed to improve. One was treated by duodenal tube administration, one by intravenous and intramuscular injections and one (empyema) by intrapleural and intramuscular administration. The patient with endocarditis improved during treatment but relapsed as soon as it was stopped. The results show that generalized staphylococcal infections can be cured by penicillin. The best method of giving the drug is by three-hourly intramuscular injections. The dose is calculated to maintain a blood concentration high enough to inhibit the growth of the infecting organism. This dose varies from case to case but is usually about 15,000 units. A rise of blood urea was observed in some patients, otherwise no evidence of any toxic effect was obtained. In bony lesions rarefaction as shown by X-rays often increased during treatment. In most cases, local application resulted in rapid elimination of the infecting organism. It must be repeated at frequent intervals so as to maintain an adequate concentration of the drug. It is necessary to continue treatment until organisms cannot be cultivated from the lesion. In eye infections it must be continued for some time after recovery, otherwise relapse often occurs. The best results are obtained when a closed cavity is present; free drainage quickly carries away the drug. Hence modifications of ordinary surgical procedures may be required, in order to establish a cavity from which discharges can be removed by aspiration and into which penicillin can be introduced. •

Pethidine hydrochloride

Clinical effects

Having administered pethidine hydrochloride by mouth to 335 patients suffering from pain, R. V. Christie speaks fairly favourably of its analgesic powers. Of the 335 patients 236 obtained complete or partial relief from doses of from 25 to 100 milligrams ($\frac{1}{2}$ to $1\frac{1}{2}$ grain). In 109 cases the effects were compared with those of compound codeine tablets (National War Formulary). Pethidine was reported in 21 per cent of cases to be equal in efficacy, in 46 per cent superior, in 33 per cent inferior. The usual dose of compound codeine tablets contained 8 grains (0.5 gramme) of acetyl salicylic acid, 8 grains (0.5 gramme) of phenacetin, $\frac{1}{4}$ grain (0.016 gramme) of codeine phosphate. In thirteen cases similar comparison with morphine showed that pethidine is inferior to that drug. Toxic effects were noted in twenty-two patients. The symptoms, which included nausea, vomiting, giddiness and 'hangover', were not in any case serious. Habituation was not observed; in one patient a dose of 50 milligrams ($\frac{3}{4}$ grain) of pethidine was repeated regularly for three months, and lost none of its efficacy and, when it was stopped, withdrawal symptoms were not observed. The danger of addiction appears to be much less than in the case of morphine. In a few cases pethidine was given by injection and seemed to be more effective than when given by mouth.

For relief of pain

Pethidine hydrochloride has been tried by A. W. Branwood in a series of twenty-three cases of pain from various causes. He found it invariably successful in relieving pain associated with muscular spasm (for example biliary colic) but almost entirely inefficacious in pain arising from other causes. Toxic effects were not noted. When given by injection pethidine

affects the circulatory system; injected intravenously it causes a rapid and considerable fall of systolic and diastolic blood pressure; given intramuscularly there is a more prolonged and steady diminution of pressure. It is thus contra-indicated in certain cases, for example in shock, in which a fall of pressure is undesirable. Intravenous injection is apt to induce dizziness and faintness.

Procaine

Subarachnoid injection

Detoxification products in the urine.—A. Goldberg, H. Koster and Rose Warshaw have studied the fate of procaine given by subarachnoid injection. A colorimetric method of measurement was employed. They confirmed the observations of other workers who have shown that procaine disappears steadily from the cerebrospinal fluid. About an hour after injection less than 10 per cent is recoverable. This might be due either to chemical change or to vascular absorption or to tissue fixation. The first possibility was ruled out; about 97 per cent of the procaine recovered from the cerebrospinal fluid at the end of an hour was unchanged. From 10 to 15 per cent of the total dose was found unchanged in the blood. The remainder appears to be detoxicated in the blood stream by enzyme action: about 90 per cent of the total dose of procaine was recovered in the form of detoxification products (para-acetaminobenzoic and para-acetaminohippuric acids and para-acetaminobenzoyl glycuronate) from the urine.

Rectal administration of nutrients and drugs

Absorption

Reports of investigations—Two papers by J. W. A. Mackenzie deal with the absorption from the rectum of nutrients and drugs. For nutritional purposes three substances were investigated, namely glucose, sodium chloride and predigested protein. Three drugs were studied—potassium bromide, sodium salicylate and sulphanilamide. (1) The absorption of glucose was studied in thirty-five convalescent children aged from five to thirteen years. Blood sugar estimations carried out before and at half-hourly intervals after the enema was administered showed that there was not any rise in blood sugar. The explanation was thought to be that glucose is absorbed so slowly that the liver is able to intercept and store it. The amount of glucose recoverable by washing out the rectum at the end of the experiment was found to vary from 7.45 to 60 per cent of the total. Fermentation was found to account for only a trifling disappearance of glucose and it is concluded that absorption accounts for most of the loss. The sparing effect on nitrogen metabolism was tried in six subjects. The latter were put on a constant low carbohydrate diet and the daily output of nitrogen was estimated. All showed distinct diminution in nitrogen excretion after the glucose enema was given but in only two was the previous excretion constant enough to render the result significant. (2) The absorption of sodium chloride from the rectum was found almost to equal that from the mouth. The daily output of chlorides rose commensurately with the amount absorbed. (3) Predigested protein was administered to three children whose nitrogen excretion had previously been stabilized. The output was found to rise by an amount approximately equal to the amount of non-protein nitrogen given. It is concluded, therefore, that the non-protein part of the enema was absorbed. (4) Potassium bromide in 1 per cent solution was given to five children. The amount excreted in the urine was found to equal the amount excreted when the drug is given by mouth. (5) Sodium salicylate similarly appeared to be absorbed with equal readiness whether it was given orally or per rectum. (6) Sulphanilamide was absorbed to some extent from the rectum when given in doses of 1 gramme dissolved in 200 cubic centimetres of water, scarcely at all when suppositories were used. Absorption is much more rapid and complete when the drug is given by mouth. Rectal administration may be preferred when oral administration causes vomiting and when it is desired to avoid the pain and possible irritating effects of intramuscular injections.

Sulphadiazine

Efficacy and toxicity—M. Finland, O. L. Peterson and R. A. Goodwin, Jun. have studied the efficacy and toxicity of sulphadiazine in a series of 460 cases of various infections. All patients who received sulphadiazine for less than twenty-four hours or to a total of under 10 grammes (150 grains) are excluded. In general the drug was given orally in an initial dose of 4 grammes (60 grains), then doses of 1 gramme (15 grains) were given every four hours, often reduced to 1 gramme every six hours after the temperature had been normal for a day or two. In cases of meningitis and some other severe infections the initial dose was 5 grammes (75 grains) given by injection; often thereafter two or more doses of 2.5 grammes (40 grains) were given in an attempt to maintain a blood level of from 15 to 20 milligrams per 100 cubic centimetres. The total dose varied greatly, some patients receiving the drug for more than five months. Haemolytic streptococcal infections, excluding endocarditis, responded well: of ninety-six patients all but three recovered. In fourteen cases of subacute bacterial endocarditis the results were disappointing; only one patient was apparently cured. Seventeen patients with *Staphylococcus aureus* pneumonia or septicaemia recovered. Three patients with Friedlander's bacillus infection were treated, of whom two recovered; in the fatal case multiple liver abscesses were found *post mortem*. All cases (twenty-four) of gonococcal infection gave a favourable response. Twenty-seven patients with bacterial meningitis were treated; all the meningococcal cases (eleven) did well; five out of eight pneumococcal patients died. Good

results were obtained in most cases of pneumococcal pneumonia and of urinary tract infections. In 33 per cent of patients toxic manifestations occurred; they were mostly mild. One fatal case of kidney damage occurred, and the importance of insisting upon a large fluid intake, especially in cases of damaged kidneys, is stressed. Aggranulocytosis occurred in one case. No evidence of sensitization was observed in patients who received repeated courses of sulphadiazine.

Sulphathiazole

Prophylactic effects in mice exposed to infection.—T. N. Harris, Harriet E. Sommer and C. C. Chapple have investigated the effects of sulphathiazole inhalations. The method used was as follows. A sulphathiazole 'smoke' was produced from a 5 per cent aqueous suspension of microcrystals by means of an atomizer. The spray was led into a chamber containing white mice. The droplets quickly dried, leaving the sulphathiazole smoke in the air. Preliminary observations were made on normal mice exposed to the smoke for varying periods. No general ill effects were observed in the mice during or after exposure, and examination of the lungs at intervals up to several days afterwards showed nothing more than slight hyperaemia soon after the inhalation. A high concentration of sulphathiazole developed in the blood. The concentrations found in the lungs when the mice were killed at the conclusion of the experiment were very low, indicating that absorption from the lung takes place rapidly. In mice exposed first to atmospheres containing influenza A virus and subsequently to atmospheres sprayed with cultures of pneumococci, the death rate of from 70 to 80 per cent was reduced by sulphathiazole inhalation to 10 per cent, and the percentage of mice which escaped pneumonia was increased from 20 to 60.

Sulphonamide compounds

Effect on eye infections

M. Klein and A. Sorsby have studied the effect of local and general sulphonamide treatment in experimentally produced infections of the eye. A difficulty encountered at the onset is that most of the organisms ordinarily concerned do not give distinctive lesions in experimental animals. For example, the only organism capable of producing classical corneal ulceration in the rabbit is *Bacillus pyocyaneus*, a clinically rare organism. Many organisms, on the other hand, will produce intra-ocular infection. In one series of experiments a raw area was produced on the anaesthetized cornea of both eyes of rabbits and a culture of *B. pyocyaneus* applied. One eye only was treated by local application of various sulphonamides. The only ones which had even a slightly beneficial effect were sulphamylamide applied under a contact lens and sulphapyridine. General (intramuscular) administration also gave negative results. In a second series of rabbits intra-ocular infection was induced by injecting streptococci or pneumococci into the anterior chamber. Again local treatment was ineffective. General administration of sodium sulphacetamide was successful in most cases of streptococcal infection. In three eyes with pneumococcal infection it was less successful, one being lost and the others showing a severe reaction. Attempted infection with staphylococci was unsuccessful.

Renal complications

In treatment of sulphadiazine.—The possibility of severe toxic reactions in the urinary tract, with or without anuria, is a disquieting feature of sulphonamide treatment and has led to continued search for a less toxic product. The claims of sulphadiazine in this respect are examined by H. S. Jeck and L. Orkin in a paper read at the annual meeting of the American Association of Genito-Urinary Surgeons. During the six months ending February, 1942 sulphadiazine has been substituted for sulphathiazole in most cases of pneumonia treated at the Bellevue Hospital, New York. The clinical results have been mainly good but the urological service has been called in consultation on over thirty-five patients (out of an unstated total of cases treated) who passed crystals of acetylsulphadiazine in the urine, with mild colic or microscopic haematuria in some cases; and for ten who developed more serious renal complications, from which three died. The purpose of the authors is to show that sulphadiazine is by no means incapable, as has been claimed for it, of causing damage to the kidney. Detailed reports are given of the ten serious cases, of which five occurred in males aged from fifty-six to seventy years, and five in females aged from fifty-two to ninety-three. Nine of the patients were admitted to hospital for lobar pneumonia or broncho-pneumonia and one, who received the drug prophylactically, for a fractured femur. All the patients showed evidence of arteriosclerotic heart disease with various degrees of congestive failure. The route of administration was oral in all cases and intravenous also in two. One patient received 32 grammes of sulphathiazole before sulphadiazine was given. The usual initial dose was 2 grammes and was followed by doses of 1 gramme every four hours. Symptoms appeared after periods ranging from three to twenty-one days, and in two instances after the drug had been stopped. The total amount of drug taken varied from 12 to 128 grammes. Thus a severe reaction may occur after only three days of treatment or a total dosage of 12 grammes. The fluid intake may not have received enough attention in these cases; it is vitally important that at least 2,000 cubic centimetres per day be taken and the urinary output must be carefully noted and not allowed to fall appreciably. Attention must also be paid to the blood level of sulphadiazine and of non-protein nitrogen, the latter being estimated at least every other day. If the urine is acid alkalis should be given freely. Important danger signals are a fall of fluid output below 1,000 cubic centimetres, a rise of blood non-protein nitrogen and microscopic

haematuria. When the sulphadiazine concentration in the blood rises above 12 milligrams precautions must be redoubled.

Sulphapyridine

Effect on kidneys.—W. A. Flynn has successfully treated eight cases of sulphapyridine anuria by massage over the kidneys and ureters with the addition of intravenous infusion of saline in some cases. In simple haematuria it usually suffices to stop the drug and give plenty of water. If anuria supervenes the same treatment may suffice provided that vomiting is not severe and an adequate amount of water can be retained. If urine has not been passed in the first half hour after treatment has been begun the patient is placed in the knee-elbow position and a finger in the rectum massages the lower ends of the ureters. The patient then lies on his back and massage over the kidneys and ureters is performed from above downwards for two or three minutes on each side. If urine is not passed an intravenous saline drip is started and massage is again applied to the lower ends of the ureters. Ureteric catheterization is resorted to if excretion is not re-established within twelve hours. A. L. Kerr reports the case of a man who developed colic and anuria after taking 21 grammes of sulphapyridine. Saline infusion had no result, so ureteric catheterization was carried out on one side seventeen hours after the onset; attempts to catheterize the second ureter were unsuccessful. An abundant flow of urine issued from the catheter and the symptoms abated. Three days later cystoscopy was performed with the intention of catheterizing the other ureter. It was found to be already excreting well, that is excretion from the corresponding kidney had re-established itself spontaneously. In a case described by W. Thompson the course of events was similar. Ureteric catheterization was performed on one side with difficulty and proved impossible on the other, owing to the blocking of the ureters by masses of solid material. Nevertheless cystoscopy forty-eight hours later showed the uncatheterized ureter excreting normally. Examination of the urine from the catheterized ureter showed gradual improvement in kidney function, the specific gravity rising from 1,006 to 1,012 in thirty-six hours, the blood urea during the same period fell from 75 to 28 milligrams per 100 cubic centimetres.

Uremic calculi in sulphonamide treatment

S. S. Sobin, L. M. Aronberg and H. C. Rolnick point out that a review of the renal changes shown by the various sulphonamide compounds in man and animals makes it clear that, with minor differences, the pathological picture is constant. From their own observations on experimental animals and a survey of the published work of others they reach the following conclusions. Intrarenal foreign material following sulphonamide drug treatment is of two forms: (1) precipitated sulphonamide and its acetylated products, (2) cellular debris, with calcium and iron deposition around or on this material. Urea simultaneously administered with sodium acetylsulphapyridine will prevent the precipitation of sulphonamides and the formation of renal calculi in rats. The action of urea is independent of a diuretic effect and depends on a specific solvent effect on acetylsulphapyridine. The nephrotoxic properties of acetylsulphapyridine are mechanical in nature and result from precipitation of the drug in the renal tract. Calcification in the kidney and the resultant calculus formation in the sulphonamide-treated animals depends upon local tissue damage and the secondary deposition of calcium and iron upon focal non-viable structure. The authors insist that a distinction should be made between the various terms applied to foreign material found in the renal tract with sulphonamide treatment. *Concretion*, *calculus*, *urolith* and *stone* have been used indiscriminately. They reserve *calculus* for those bodies with a mineral content, especially calcium, and *concretion* for any solid body. *Urolith* and *stone* by derivation imply a mineral or calcium content.

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PHYSIOTHERAPY

Use in various medical conditions

G. M. Piersol, speaking at the American Congress of Physical Therapy, dwelt upon the possibilities of physical methods of treatment for various medical conditions. In selected cases physiotherapy is a most valuable adjunct to treatment. In arthritis and allied disorders massage, exercises and heat are often highly beneficial, though care must be exercised in the application of general heat, which is not suitable for every case. In the convalescence period after acute illness physiotherapy helps to restore health. Cardiovascular disease offers a promising field for the use of graduated exercises and suitable hydrotherapy. Artificial fever treatment has yielded good results in neurosyphilis and gonorrhoea.

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PINK DISEASE

See also B.E.M.P., Vol. IX, p. 603; and Cumulative Supplement, Key No. 1261.

Treatment

Liver

Hepatex injections.—C. Pinckney reports three cases of pink disease. The patients were all females, aged respectively nine, ten and twelve months. In each case the child was miserable, with loss of appetite, photophobia, pink and desquamating hands and feet, tachycardia and flabby muscles. Two children had a rash. One was treated at first by vitamin B which was given by mouth without effect, and was then given liver injections (Hepatex, 1 cubic centimetre) twice weekly. After four weeks' treatment she was cured and discharged from hospital. The other two patients were treated by Hepatex from the beginning, both recovered after injections of 1 cubic centimetre which were given twice weekly for four weeks.

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PLACENTA: DEVELOPMENT AND DISEASES

See also B.E.M.P., Vol. IX, p. 641.

Development of embryo and membranes

Embryo

Respiration in the foetal sheep.—J. Barcroft, in his Linacre lecture, describes experiments made to study the evolution of respiration in the foetus of the sheep. If a pregnant ewe under spinal anaesthesia is immersed in a saline bath at body temperature and the amniotic sac exposed, the foetus can be seen through the transparent walls and can be studied at different ages. Movements begin on about the thirty-fifth day when, in response to a tap at a particular point on the face, the head is retracted. Each day afterwards the number of points from which the movement can be elicited and the number of muscles involved, increase. By the thirty-eighth day the diaphragm becomes active. The next stage shows a rhythmic discharge in response to a single stimulus. The intercostal muscles are first seen to contract during this stage, which begins on about the fortieth day. The muscles of respiration are those which continue longest in rhythmic contraction. By about the forty-fifth day the response to stimulation consists in an initial 'writhe' of the body with subsequent movements of the respiratory muscles; and later still a pause, becoming longer as gestation proceeds, intervenes

between the two phases. By fifty days movements can be elicited by stimulation of most parts of the body; at this stage asphyxia produced by occlusion of the umbilical cord never initiates a respiratory rhythm, which seems to be governed exclusively by the central nervous system. A phase of inhibition now sets in; by the sixtieth day the foetus is completely inert and makes little or no response to considerable stimuli; but if the cord be occluded respiratory movements immediately begin. Further experiments were carried out in which the brain of one of twin foetuses was transected; this procedure did not affect growth. It was carried out after the sixtieth day and observations were made about two weeks later; they showed that the seat of inhibition is anterior to the pons, but changes position at different ages, being higher up the brain in the older foetus. At birth two things happen; inhibition is depressed by asphyxia and the brain begins to receive volleys of sensation. If sensation be sufficiently depressed, inhibition becomes dominant and respiration is slow in starting. The antagonism between inhibition and sensation was demonstrated by delivering the foetus after fully anaesthetizing the ewe. It was found that the sensory stimulation provided by a stream of oxygen directed on to the foetus's face was a highly successful method of initiating respiration.

Barcroft, J. (1942) *Lancet*, 2, 117.

PNEUMONIA, LOBAR

See also B.E.M.P., Vol. IX, p. 713; and Cumulative Supplement, Key No. 1279.

Aetiology and bacteriology

Types of pneumococci

An analysis of cases in Montreal.—J. C. Meakins and R. D. McKenna analyse twenty-one fatal cases of pneumococcal lobar pneumonia in patients treated in the Royal Victoria Hospital, Montreal, during the years 1940–2. The total number of pneumonia cases admitted in that period was 200. The type of pneumococcus responsible was type I in thirty cases, with three deaths; type II in thirty-nine cases, with one death; type III in thirty-nine cases, with nine deaths; type IV in twelve cases, with one death; type V in nineteen cases, with one death; type VI in eight cases, with one death, type VII in eighteen cases, with two deaths; type XI in six cases, with two deaths, type XIV in three cases, with one death. In the remaining twenty-six cases types XII, XVII, XVIII, XIX, XX, XXIII, XXIV and XXVII were responsible and there was not any associated mortality. The mortality rate in the two sexes was identical. The incidence was much heavier in males—76 per cent of all cases. Excluding infants, no deaths occurred in people under forty years old. The average age in the fatal cases was 56.6 years, of the survivors 36.1 years. Bacteraemia was proved by blood cultures to be present in twelve of the twenty-one cases. The number of lobes involved was as follows: in six cases, one lobe; in eight, two lobes; in four, three lobes; in three, four lobes. Eleven of the patients showed evidence of cardiovascular disease; five had advanced emphysema; one patient had diabetes mellitus, and one was a chronic alcoholic. Malnutrition was pronounced in eleven cases. Thus of the fatal cases, 90 per cent showed associated disease, of the survivors, only 32 per cent showed comparable diseases. Early chemotherapy is of great importance and should be supplemented by serum if the prognosis seems poor. Anti-shock therapy may save some patients; seven in the authors' series showed signs of circulatory collapse and in none of these were modern methods of treatment used.

Pathogenesis and morbid anatomy

Pathogenesis

Experimental infection in dogs.—O. H. Robertson discusses the mode of origin of pneumonia. Organisms may gain access to the lung as the result of inhalation of droplets or of the entry of fluids into the larynx. Air-borne infection appears to be relatively uncommon; contacts rarely develop the disease and attempts to produce infection in animals by exposing them to atmospheres containing infected droplets have been unsuccessful. One instance of infection in a laboratory assistant as the result of accidental exposure is known to the writer. The more important mode of infection would seem to be the entry into the lungs of infective material derived from the upper respiratory passages. The ciliary mechanism of the air passages is much less well adapted to deal with liquid than with solid particles; liquids dropped into the air passages of animals are found in a short time in the depths of the lungs. Moreover the efficiency of the ciliary mechanism depends upon an intact mucous layer. The epiglottis is not a perfect barrier. Conditions which cause it to fail to close completely have not yet been fully ascertained, but in rats cold has been shown to be a factor. The author has succeeded in producing lobar pneumonia regularly in dogs by injecting a suspension of pneumococci and starch into a terminal bronchus after giving morphine in sufficient doses to lower the body temperature by from three to five degrees. Secondary lesions were artificially induced in different parts of the lung by placing the dogs in different positions. That irritation plays a part in the development of the disease was shown by substituting the animal's own citrated plasma for the starch vehicle in some experiments; animals receiving this non-irritating suspension did not develop pneumonia unless very large doses of pneumococci were given. The danger of pneumonia after general anaesthesia, especially in the presence of upper respiratory infection, is explained by the experiments recorded.

Lipid pneumonia due to iodized oil.—As it has been suggested that the use of iodized oil may predispose to collapse of the lung after lobectomy, J. T. Chesterman investigated this question

in twenty-five cats which were anaesthetized with intraperitoneal injection of nembutal (pentobarbital sodium), and amounts of iodized oil up to 5 cubic centimetres were injected through an intratracheal catheter; the animals were then examined from one day to thirty-two weeks later. In the interim some of the cats underwent lobectomy. In three cats lipid pneumonia occurred; in all of these the form of iodized oil injected was viscous neo-hydriol (iodized oil). The eight cats injected with lipiodol (iodized oil) and the six cats injected with iodatol (iodized oil) did not show lipid pneumonia. The change consisted of yellow areas of consolidation composed of polymorphonuclear leucocytes, large phagocytic cells each containing oil globules, and proliferated epithelium.

Complications and sequelae

Gastro-intestinal

Associated jaundice.—M. Gelfand and Beryl Lewis state that in natives of Mashonaland pneumonia is often associated with jaundice; the incidence is about 18 per cent, and it is important in examining a jaundiced native to bear the possibility of pneumonia in mind. Of ten patients examined six gave a biphasic and two an indirect response to the van den Bergh test, indicating some toxic action, probably on the liver. It may be that a particular haemolytic strain of pneumococcus is liable to affect the native. The jaundice is intense, of rapid onset and almost equally rapid disappearance and does not influence the prognosis.

Treatment

Non-specific

Sulphadiazine—H. K. Ensworth, M. Kalkstein, S. W. Barefoot, J. Liebmman and N. Plummer have used sulphadiazine in the treatment of 239 patients with pneumococcal pneumonia. The advantage of this drug over sulphapyridine is its relatively low toxicity, and it appears to be at least equal in therapeutic value to sulphapyridine. The sulphadiazine was given orally in most cases. The initial dose was 2 grammes (30 grains) and further doses were of 1 gramme (15 grains) given every four hours. The death rate for the whole group was 10.9 per cent or, if deaths within the first twenty-four hours are excluded, 7.8 per cent. Positive blood cultures were obtained in forty-two patients among whom the death rate was 30.9 per cent or, if deaths within the first twenty-four hours are excluded, 21.6 per cent. The numbers of each kind were insufficient to show the relation of pneumococcal type to mortality. The death rate rose from 6.5 per cent in patients who had been given treatment within the first three days, to 9.0 per cent in patients who had been ill for more than three days before beginning treatment. The influence of age was shown by the fact that the death rate under thirty years was nil, between thirty and fifty years it was 1.2 per cent, and from fifty years onwards it was 14.4 per cent. The toxic effects observed included vomiting in five patients, leucopenia in four, anaemia in one, rash with fever in four, fever alone in two, haematuria in five (with renal colic in one), and partial deafness in one. The number of complications that were seen was small.

Chesterman, J. T. (1942) *J. Path. Bact.*, **54**, 385.

Ensworth, H. K., Kalkstein, M., Barefoot, S. W., Liebmman, J., and Plummer, N. (1942) *Amer. J. med. Sci.*, **204**, 179.

Gelfand, M., and Lewis, Beryl (1942) *S. Afr. med. J.*, **16**, 436.

Meakins, J. C., and McKenna, R. D. (1943) *Canad. med. Ass. J.*, **48**, 104.

Robertson, O. H. (1943) *Ann. intern. Med.*, **18**, 1.

POLIOMYELITIS AND POLIOENCEPHALITIS

See also B.E.M.P., Vol. X, p. 12; and Cumulative Supplement, Key No. 1282.

Aetiology

In nasopharynx

Infection after tonsillectomy.—T. Francis, Jun., C. F. Kill, J. A. Toomey and W. N. Mack report an incident illustrating the danger of performing tonsillectomy in children during the season in which poliomyelitis occurs, even although the disease may not be noticeably prevalent at the time. Of a family of six children, aged from eleven to two and a half years, all but the youngest underwent tonsillectomy and extraction of teeth during the month of August, 1941. Nine days later all the five children developed, within a space of forty-eight hours, symptoms of bulbar poliomyelitis from which three subsequently died. Only two recent cases of poliomyelitis had occurred in their home town, and contact could not be established with them. There was not an epidemic subsequently, although six additional cases developed in the town during September. In order to determine the source of infection, monkey inoculation tests were carried out using house flies, dust from bedrooms, and water from a neighbouring pond; all were negative for the virus. Specimens of faeces were obtained from fifty-four persons with whom the children had associated, and were tested in the same way. The virus was demonstrated in ten of these specimens. The positive stools came (1) from two cousins in another town with whom two of the children had stayed a month before, and from whom it was thought that the infection was most probably acquired; (2) from four other cousins belonging to a different family with whom the children had stayed subsequently; (3) from three children of one family, playmates of the affected children; and (4) from the youngest child of the affected family, the only one who did not undergo operation and who

never showed signs of infection. It appears clear that tonsillectomy was the factor which precipitated infection in the children carrying the virus of poliomyelitis.

Clinical picture

The paralytic stage

New concepts.—M. E. Knapp discusses the three basic ideas which characterize the Kenny conception of infantile paralysis. (1) Muscular spasm of unknown origin can be observed in the first few days of the disease and differs from the spasticity of an upper motor neurone lesion in failing to relax under steady traction. Fibrosis and contractures may follow, possibly owing to the anaemia caused by the spasm. (2) Mental alienation appears to represent a physiological as contrasted with an anatomical blocking of conduction. The psychological explanation favoured by Sister Kenny may not entirely account for this phenomenon. (3) Incoordination means first that abnormal motor patterns are developed, in the form either of substitution or of 'spilling over' of impulses to non-related, even to antagonistic, muscles; and secondly that a muscle may contract in part only instead of in its whole extent.

Treatment

The paralysis

The Kenny treatment.—F. H. Krusen's conclusions on the Kenny treatment of poliomyelitis are based on two years' observation of cases which were treated by her method. In preliminary interviews with Sister Elizabeth Kenny it was found that much of her terminology was peculiar to herself; her words could not be understood in their usual sense, but several American authorities, including A. Steindler, I. A. Russin, L. Sheplan and V. Wolkin, have confirmed some of her observations. The Kenny theory of poliomyelitis requires that for the conception of a primary flaccid paralysis, there must be substituted one of a condition of muscular irritability with spasm. Other major symptoms are 'incoordination', consisting in ineffective contractions or delegation of function by one muscle to another and 'mental alienation' or inability to contract a muscle voluntarily. Treatment consists in the application of hot packs to relax spasm and when this has been achieved, in mental re-education to induce the patient to move the muscle actively. The author thinks that Sister Kenny's observations are correct and that her method of treatment deserves trial.

P. M. Stimson points out that, in acute anterior poliomyelitis, several factors cooperate in causing muscular dysfunction. The action of the virus on the motor neurones is not necessarily totally destructive; some neurones are affected temporarily, and during their recovery the muscle fibres governed by them are subject to spasm, which causes pain and tenderness of the affected muscles, over-stretching of the antagonist muscles, and sometimes, permanent contractures. In addition, patients tend to substitute for a paralysed or spasmodically contracted muscle some unsuitable or inefficient muscle. Lastly, mental influences may interfere with the proper use of surviving neuromuscular units. Paralysis due to complete destruction of the motor neurones is irremediable, but the Kenny treatment can rescue surviving units from the effects of the other factors. In the early stages patients should be subjected to as little handling as possible; limbs should not be splinted and massage and electrotherapy should be avoided. Patients who are obviously ill and dehydrated should be given intravenous infusions of glucose-saline. Spasm should be treated by application of hot fomentations, especially the spasm of the diaphragm, pectoral and intercostal muscles, which is often the principal cause of difficulty in breathing and which is aggravated by the use of mechanical respirators. Spasm also plays an important part in disturbances of swallowing, micturition and defaecation, and can be similarly relieved by hot fomentations. After a few days passive movements are begun and, when spasm is no longer present, active movements are allowed. From the onset, the patient must be encouraged to adjust himself to his disabilities.

Francis, T., Jun., Krill, C. E., Toomey, J. A., and Mack, W. N. (1942)

J. Amer. med. Ass., **119**, 1392.

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Knapp, M. L. (1942) *Arch. phys. Ther.*, **23**, 668.

Krusen, F. H. (1942) *Proc. Mayo Clin.*, **17**, 449.

Steindler, A., Russin, L. A., Sheplan, L., and Wolkin, V. (1942) *Arch. phys. Ther.*, **23**, 325.

Stimson, P. M. (1942) *J. Amer. med. Ass.*, **119**, 989.

PREGNANCY: NORMAL AND PATHOLOGICAL

See also B.E.M.P., Vol. X, p. 48; and Cumulative Supplement, Key Nos. 1291–1303.

Hyperemesis gravidarum

Treatment

Injection of husband's blood—W. L. Hughes and A. C. Martin report the case of a pregnant woman who in previous pregnancies had suffered from hyperemesis gravidarum and who remained free from vomiting while receiving intramuscular injections of her husband's blood. The rationale of the treatment was that, since the patient suffered after coitus from headache similar to that caused by certain foods, first that she might be sensitive to her husband's tissues, and secondly that the tissues of the foetus might be similar to those of its father and might be incompatible with the mother's tissues. She had had seven previous pregnancies, in

all of which she had suffered from severe and intractable vomiting and had been in bed most of the time. Injections of 2 cubic centimetres of the husband's blood were given throughout the eighth pregnancy, at intervals of from two to fourteen days, depending upon the patient's symptoms. On one occasion 3 cubic centimetres of the patient's own blood was substituted for that of the husband, without relief. It was noted that if the husband had taken any of the foods to which the patient was sensitive, she suffered from headache after receiving his blood. The patient was able to be up and about until the thirty-fourth week. At the thirty-sixth week the blood pressure and blood urea rose and toxæmia was considered to be developing. Labour was therefore induced and a living child was born. The blood groups of the husband, the child and the patient were determined. The patient belonged to group O, whereas the husband and child belonged to group A.

Vitamins B₁ and B₆—Observations on the treatment of nausea and vomiting in pregnancy by vitamins B₁ and B₆ are recorded by R. S. Willis, W. W. Winn, A. T. Morris, A. A. Newsom and W. E. Massey. Vitamin B₁ was used in one series of patients and vitamin B₆ in another. The preparations were given either by intramuscular or by intravenous injection in varying doses (10 to 100 milligrams, $\frac{1}{2}$ to 1½ grains) and at irregular intervals, according to the reappearance of symptoms; the number of injections varied from one to thirty. Relief was obtained in most cases whichever vitamin was given, but it was more constant and more complete after vitamin B₆ administration than after vitamin B₁ administration. Undesirable reactions were not noted. Control experiments were not carried out, and it is not stated which actual vitamin preparations were used.

Toxaemias of late pregnancy

Pre-eclamptic toxæmia and eclampsia

Prevention of eclampsia.—N. J. Eastman and J. Whitridge, Jun. lay down the following rules for the prevention of eclampsia (1) Expectant mothers should undergo medical examination not later than after the second missed period and thereafter every four weeks during the first five months, every two or three weeks during the next three months and every week during the last month. (2) Frequent and regular blood pressure readings are all-important. (3) Sudden gain in weight of more than two pounds in a week is a suggestive, and of more than three pounds an alarming, sign, since it represents latent oedema. (4) The sudden appearance of albumin in the urine should be regarded as a sign of impending eclampsia. (5) Patients must be adjured to report to the doctor immediately there occurs any severe headache, swelling of face or fingers, visual disturbances, persistent vomiting, diminished excretion of urine or epigastric pain. If any sign of incipient toxæmia develops, blood pressure readings should be made often, that is at least once and, if necessary, two or three times, a week. Complete rest in bed is desirable in most cases. Salt intake should be restricted by leaving it out of the food, either in the kitchen or at the table. Meat is permitted. A saline purgative should be given at the outset of treatment and repeated twice weekly. The fluid intake should be from four to five pints daily. A sedative such as phenobarbitone should be given or, if convulsions appear to be imminent, paraldehyde in large doses. Should the toxæmic condition continue to progress, termination of pregnancy should be undertaken. If eclampsia develops figures show that heroic operative treatment is lethal and that the best chance for the patient lies in darkness, quiet and sedatives, of which paraldehyde in rectal doses of 30 cubic centimetres at the start, followed by 15 to 20 cubic centimetres as often as is necessary, is one of the best. Persistent hypertension demands subsequent sterilization.

Essential hypertension

Clinical picture.—In a paper read before the Washington Obstetrical Society R. D. Mussey, A. B. Hunt and F. S. Sluder consider the implications of hypertension in pregnancy. Hypertension may be present as a result of pre-existing vascular and renal disease or of toxæmia of pregnancy. In some cases both factors may operate. The former is associated with generalized arteriosclerosis, the latter with acute vasospasm only. The spasm of the arterioles is probably due to the action upon the vessel wall of some pressor substance circulating in the blood. The spasm has been directly observed in the arterioles of the retina. Chronic cardiovascular and renal disease tends to be aggravated by pregnancy, and sometimes acute toxæmic hypertension is superimposed. Symptoms due to chronic hypertensive disease almost always appear before the twenty-fourth week of pregnancy whereas symptoms of acute hypertensive disease are usually evident after that date. Chronic hypertension is commonly associated with enlargement of the heart and obvious changes in the retinal vessels and occasionally with evidence of impaired renal function. The blood pressure remains above 160/100 millimetres Hg in spite of rest. In some cases signs of nephrosclerosis predominate. The urine contains albumin, usually in moderate amount, and the specific gravity is below 1022; albuminuric retinitis may be present; when the condition is advanced the non-protein nitrogen content of the blood is raised. It may, however, be extremely difficult to decide whether hypertension and other symptoms are due to pre-existing chronic vascular disease or to acute hypertensive toxæmia. The former tends to occur in multiparae over thirty, the latter in primiparae of under thirty and usually under twenty-five, years of age. Treatment involves careful and continuous supervision. In chronic hypertension the woman should have the right to take the risk of allowing the pregnancy to continue unless her life is considered to be endangered thereby.

Diseases of the cardiovascular system**Heart disease**

Rheumatic heart disease complicating pregnancy.—Sixty-one fatal cases of rheumatic heart disease complicating pregnancy have been studied by G. L. Hoffman, Jun. and W. A. Jeffers, with special reference to the possibility of prevention. Failure of cardiac compensation accounted for 64 per cent of the deaths, embolism or other sudden catastrophe for 16 per cent and puerperal sepsis with terminal heart failure for 15 per cent; the remaining three patients (5 per cent) died, one from subacute bacterial endocarditis, one from acute endocarditis and one from unascertained causes. In 85 per cent of the cases death occurred after the twenty-eighth week and in 67 per cent after the thirty-fifth week of pregnancy. In 79 per cent delivery had already taken place, and of these patients 48 per cent died in the first twenty-four hours of the puerperium. Only 5 per cent of the deaths occurred during labour, and little evidence was obtained that labour seriously increases cardiac distress. About half the number of patients were delivered by Caesarean section. In the cases in which death occurred after delivery, it was shown that the state of the heart at the onset of labour was an important factor; the death rate was lowest in the patients who had maintained cardiac compensation throughout pregnancy and was highest in patients who were suffering from congestive heart failure at the time of delivery. Prenatal care of the heart offers the best hope of reducing the death rate. Vaginal delivery is in most cases preferable to Caesarean section which causes a heavy mortality from sepsis in patients with cardiac disease.

Eastman, N. J., and Whitridge, J., Jun (1942) *J Amer med. Ass.*, **120**, 729.

Hoffman, G. L., Jun., and Jeffers, W. A. (1942) *Amer. J. med. Sci.*, **204**, 157.

Hughes, W. I., and Martin, A. C. (1942) *Amer. J. Obstet. Gynec.*, **44**, 103.

Mussey, R. D., Hunt, A. B., and Sluder, F. S. (1943) *Amer. J. Obstet. Gynec.*, **45**, 224.

Willis, R. S., Winn, W. W., Morris, A. T., Newsom, A. A., and Massey, W. E. (1942) *Amer. J. Obstet. Gynec.*, **44**, 265.

PRICKLY HEAT

See also B E M.P., Vol. X, p. 139.

Clinical picture**The rash**

Clinical types of eruption.—D. M. Blomfield draws attention to the various forms which prickly heat may take in Europeans, and to the fact that the condition is sometimes serious. Severe cases were seen among troops in Assab in southern Eritrea where conditions that give rise to prickly heat are prevalent in July and August: this area lies in one of the four hottest zones in the world and during the hottest months the climate is very humid. Other causal factors are the length of time spent in the area and an inadequate diet. Assab was cut off during July and August, 1941 from supplies of fresh food, and the resulting lack of vitamins probably influenced the incidence and course of the disease. The cases of prickly heat seen were of various clinical types, roughly in the order of frequency and also in the order of progression in the individual case, as given below: (1) In the miliarial type a bright red rash suddenly appeared in various parts of the body, associated with sensations of pricking and irritation. (2) In some cases a special form of boil occurred on the fingers. It developed slowly and insidiously and after the exudate had escaped the skin peeled off leaving a raw red surface. (3) The impetiginous type, as also type 2, should be regarded as a complicated form rather than as true prickly heat. The whole beard and moustache area was usually involved. (4) The pemphigous type, apparently a true form of prickly heat, was characterized by the development overnight of symmetrical crops of blebs and bullae in the axillae and groins. (5) In a later stage of the foregoing type individual blisters, mostly in the axillae, became pustular, many showing a black centre. These black areas were probably caused by superimposed infection with the fungus *Microsporon mansonii*, but diagnostic facilities were lacking to verify such supposition. The author thinks that prickly heat represents a reaction of the sweat glands to a hot climate, dysfunction of the small sweat glands causing the miliarial type, dysfunction of the large sweat glands giving rise to the pemphigoid type of the disease. He suggests that the unsatisfactory term, prickly heat, or the equally inaccurate term, lichen tropicalis, should be replaced by the name, climatic hyperidrosis. Measures to keep the skin reasonably dry, for example by constant use of a towel to mop away sweat, and restriction of fluid intake, with antiseptic washes, are the best palliative measures available. Diet should be attended to. In severe cases evacuation to another climate is advisable.

Blomfield, D. M. (1943) *Trans. R. Soc. trop. Med. Hyg.*, **36**, 239.

PROSTATE DISEASES

See also B.E.M.P., Vol. X, p. 146; and Cumulative Supplement, Key No. 1308.

Simple enlargement**Treatment**

Importance of transurethral route.—G. J. Thompson, J. L. Emmett, E. N. Cook and T. L. Pool report on transurethral surgery in 1940 and 1941 and refer to 4,302 patients. Thompson and Bumpus in 1931 performed transurethral prostatic resection on eighty-seven patients.

During 1941 the universal application of the transurethral operation was indicated by the fact that not a single patient was treated by perineal or suprapubic prostatectomy at the Mayo Clinic. This should convince the most sceptical that even in the case of the patient with a very large prostate, relief by a transurethral operation is now possible. In 1940 and 1941 the average age of the transurethral patients was 66.2 years, and eighty-five patients, or 4.3 per cent, were eighty years of age. Only two out of the patients in the eighties died as a result of the operation. During 1940 there were sixteen deaths, or 1.6 per cent deaths among 976 operations, and during 1941, eleven, or 1.1 per cent deaths among 991 operations. Treatment of 139 bladder tumours was carried out by transurethral means in 1940 and 1941.

Perineal prostatectomy.—According to E. Davis, the public is becoming better educated in the matter of prostatic enlargement and the surgeon now sees a much higher proportion of cases of conspicuously good operative risk, in which one-stage operations are justifiable. Acute retention is becoming rare. The author cites details of twenty-four consecutive cases of perineal prostatectomy without preliminary suprapubic drainage. The average age of the patients was sixty-seven years; none had seriously impaired renal function. The average length of stay in hospital was sixteen days. Only one patient had a post-operative temperature of more than 101° F. All were operated on under sacral block anaesthesia and morphine $\frac{1}{4}$ grain (0.016 gramme), with meticulous care in suture and ligation of bleeding points and obliteration by suture of the prostatic cavity. Sulphathiazole 5 grammes (75 grains) was placed in the incision before closure and 0.5 gramme (8 grains) was given orally four times a day for ten days. Recovery was uneventful in all cases.

Post-prostatectomy obstruction.—T. Millin, discussing post-prostatectomy obstruction, states that none of the usual operations appears to be more liable than another to be followed by the above complication, the incidence of which is about 2 per cent. Early instrumentation and post-operative care in minimizing infection should prevent many such cases. The following are the main causes: (1) Membrane formation, due to 'cross union' of the torn edges of mucous membrane, and possible only when early post-operative instrumentation is not employed; (2) Scarring; this usually involves the vesical outlet with 'shelf' formation, the reason for which is not clear; early instrumentation may prevent it. Patients with early fibrous tissue obstruction are usually curable by dilatation, later cases may require endoscopic resection or even (when the obstruction is at the bladder outlet) suprapubic operation. (3) Adenomas, which are either left behind at operation or which grow later from the prostatic capsule; urethroscopy is essential for diagnosis, and endoscopic resection is usually possible. (4) Calculi; if stones have been present before operation, routine X-ray examination three months afterwards is wise. Urinary infection must be treated and the urine should be kept acid. (5) Carcinoma of the prostatic bed, which may develop years after prostatectomy has been performed for an apparently innocent enlargement, or sooner when a malignant prostate gland has been removed. Endoscopic resection may suffice to give relief, or permanent suprapubic cystostomy may be necessary. (6) Acute or chronic inflammatory lesions of the urethra, for example peri-urethral abscess leading to stricture, acute cases usually respond to conservative measures, chronic conditions to dilatation. (7) Stricture of the external urinary meatus, which requires dilatation or meatotomy. (8) Papilloma of the bladder outlet or urethra. (9) Carcinoma of the urethra. (10) Psychogenic causes which occasionally produce acute retention.

Malignant disease

Clinical picture and diagnosis

The importance of early diagnosis.—C. D. Creevy urges that more attention should be paid to carcinoma of the prostate gland because its incidence is increasing and the prognosis is not good. Early cases are still very rare and the operability rate is low. The reasons for late discovery of the disease are (1) that it is symptomless until it produces obstruction or gives rise to pain from local extension or from metastases; (2) that since in 75 per cent of cases it starts posteriorly, obstruction occurs late; (3) that growth is slow; (4) that it may develop in an already enlarged prostate gland; (5) that men are apt to regard some degree of urinary difficulty as a necessary concomitant of advancing years; and (6) that the doctor may fail to recognize the seriousness of an isolated hard nodule in the prostate gland. In its earliest clinically recognizable stage the growth appears as a small ill-defined irregular stony hard nodule. The differential diagnosis must exclude tuberculosis which is usually accompanied by frequency, urgency and pyuria, and presence of prostatic calculi, which are visible in the X-ray film; they may co-exist with a carcinoma. Sometimes an X-ray film taken to exclude a stone shows metastases in the pelvic bones, of which elevation of the serum phosphatase is a confirmatory sign. A nodule, if of chronic inflammatory origin, may clear up under a course of local heat treatment. If it fails to do so biopsy is indicated. When an early neoplasm is located in the posterior lamella a satisfactory specimen can be obtained, in the author's opinion, only through a perineal approach. Radical prostatectomy with removal of a circle of bladder wall offers the only reasonable hope of a cure and is not associated with the risk of subsequent obstruction, which is the bane of all other methods. Radon or X-ray irradiation may occasionally bring about a cure. Castration relieves the severe pain occurring late in the disease. Oestrogen therapy is still on trial.

The part played by testicular androgens.—C. Huggins, Professor of Surgery, University of Chicago, reviews the diagnosis of primary carcinoma of the prostate gland, which causes the

death of about 5 per cent of men over fifty years of age. From routine necropsies pathologists have recognized a group of miniature silent carcinomas of the prostate which occur in from 14 (Rich) to 46 (Baron and Angrist) per cent of men over fifty years of age. The symptoms of ordinary carcinoma of the prostate are tabulated as follows: increased frequency, 86 per cent; diminished urinary stream, 78 per cent; loss of weight, 58 per cent; lumbar pain, 40 per cent; and sciatica, 36 per cent. Metastases always occurred in the pelvis when they were present in bones and were never met with distal to the knee and elbow. In fifty patients with advanced prostatic carcinoma bony metastases were found radiologically in thirty-one, usually both osteoblastic and osteolytic forms; in two patients were osteolytic lesions only present. The chief confusing condition from a radiological point of view is osteitis deformans; in osteitis deformans the trabeculae of bone become increasingly gross; in carcinoma of the prostate the trabeculae of bone disappear, being incorporated in dense osteosclerotic masses. The essential criteria for the pathological diagnosis are anaplasia and invasion. In differentiating carcinoma primary in the prostate from cancer of the bladder or other part in the neighbourhood valuable help is often given by staining the tissue for acid phosphatase by the technique of Gomori, since prostatic epithelium contains much larger amounts of these enzymes than do other tissues. So far as serological diagnosis of prostatic carcinoma is concerned, A. B. Gutman and I. B. Gutman found that the latter contains phosphatase, of which there are two forms, acid and alkaline, which can split monophosphoric esters to form inorganic phosphorus. Acid phosphatase values of blood serum are significantly raised only in cancer of the prostate. Huggins believes that it has now been established that the cells of prostatic carcinoma flourish in the presence of physiologically effective amounts of male sex hormones, and often retrogress more or less, when the testicular androgens are eliminated by bilateral orchiectomy or are neutralized by oestrogen administration. The course of the disease can be well followed by frequent serial phosphatase determination

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PRURITUS AND PRURIGO (HEBRA)

See also B E M P., Vol. IX, p. 165

Pruritus

Clinical investigation

General pruritus and blood cholesterol—It is known that blood sugar and blood urea values may be raised in cases of generalized pruritus without evidence of impaired hepatic or renal function. Since these phenomena are observed in only about half the number of cases, Anne F. Somerford decided to examine the blood cholesterol values. In a series of fifty-six patients suffering from generalized pruritus with no dermatological cause she found raised blood sugar values in twelve cases and raised blood urea value in one case. The blood cholesterol of the remaining forty-three, including twenty-one males and twenty-two females, was estimated by Bloor's method. It was found to be normal in seventeen, decreased in six and increased in twenty, that is in over 60 per cent. The increased cholesterol values ranged from 242 to 586 milligrams per 100 cubic centimetres of blood, averaging 344 milligrams. None of the patients gave an allergic history nor were any obese.

Treatment

Oestrogen therapy in primary senile pruritus—S. Feldman, J. Pollock and A. R. Abarbanel, having observed that oestrogen therapy for senile vulvovaginitis, leukoplakia and kraurosis vulvae had a beneficial effect not only on the local lesions but also on the associated pruritus, have used sex hormones in cases of primary senile pruritus, on the assumption that the condition is due to endocrine deficiency. They report twelve cases, in all of which good results were obtained. In the first case eight small pieces of skin were removed for examination before and after treatment; the first sections showed oedema of the entire cutis, and haziness and diminished staining capacity of the cells of the stratum germinativum; the histological appearances in the second set of sections were much more normal. The patients, seven men and five women, ranged in age from sixty-three to eighty-eight years. Five of the men were treated by injections of 10 milligrams of testosterone propionate given at intervals of from five to fourteen days, the dose being reduced to 5 milligrams when improvement began. In one case after numerous injections had failed, a pellet of 20 milligrams of testosterone propionate was inserted beneath the skin, and in the sixth case insertion of a pellet was the only treatment given. As a control, one man who had relapsed was given three injections of 1 milligram of oestradiol dipropionate at weekly intervals, without improvement. For the women the treatment consisted of injections of 1 milligram of oestradiol dipropionate, repeated every five to seven days. As controls, two women were given several injections of

testosterone propionate; the itching was not relieved, but yielded to treatment by oestradiol dipropionate. In one case the substitution of sesame oil for the usual injection (to obviate the possible influence of suggestion) caused increased itching. In one woman uterine bleeding occurred after oestradiol administration, but was checked by combining it with testosterone. Oestradiol benzoate proved less effective than the dipropionate.

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PSORIASIS

See also B E M.P., Vol. X, p. 187; and Cumulative Supplement, Key No. 1312.

Clinical picture

General review

Importance of cholesterolaemia.—Facts and theories concerning the origin, nature and treatment of psoriasis are marshalled by E. Pulay. Chief in importance is the discovery that cholesterolaemia and a similar increase in lipoids in the affected areas of skin are constant concomitants of psoriasis. Cholesterolaemia is to be regarded as an expression of lack of both adrenal cortical hormone and vitamin B₁. The ferment which is indispensable for oxygen utilization by the tissues is not formed in the absence of adrenal cortical hormone, and the latter again is closely related to vitamin B₁. Deficiency of respiratory ferment will interfere with protein breakdown and glycogen formation. Both glycogen and tyrosine, the product of protein catabolism, are essential for normal keratinization, and tyrosine for the production of melanin. Changes in the electrical potential of the skin also result from the abnormal metabolic processes. The function of the adrenal cortex depends in its turn upon the anterior lobe of the pituitary gland. Psoriasis is the reaction to an allergic stimulus of skin which is in an abnormal condition as the result of a general metabolic disturbance. Infection, particularly with *Bacillus coli*, may provide the exogenous factor. The author has observed cholesterolaemia, hyperproteinæmia, indicanuria and creatinuria in almost every case of psoriasis. The erythrocyte count is usually raised and haemoglobinaemia is often found. Fatigue is present and there is a constant tendency for the patient to fall asleep. Patients often complain of muscular pain, which, like the fatigue, is referable to disturbance of glycogen metabolism and lack of corticotrophic hormone. In the majority of cases the liver function is altered. The sexual hormones also influence the disease. Treatment includes a diet low in proteins and fats; administration of anterior pituitary, cortical and female sex hormones and of vitamins B, C and K, and vaccine therapy in cases in which infection is thought to play a part in the aetiology.

Treatment

Goeckerman treatment

Results in two thousand cases.—P. A. O'I eary in a paper read before the Canadian Medical Association details his experiences with the Goeckerman treatment for psoriasis. This treatment necessitates the admission of the patient to hospital. On the first day a crude coal-tar ointment (2 to 4 per cent) is applied thickly, and left on over night. Iodine and the scalp salicylic acid ointment is substituted. In the morning it is removed with light mineral oil, of which a film is left on the skin. Ultra-violet light is then given to the whole body for one minute at 30 inches distance. After the light treatment the patient spends half an hour to two hours in an oatmeal bath at 95° F. This loosens the scales and allows the patient to rub them off while he is in the bath. After the bath the ointment is again applied and a second coat is given at bedtime. This routine is repeated daily, the period of exposure to ultra-violet light being increased and the distance decreased each day. Autohaemotherapy is given at two-day intervals for five doses, 5 cubic centimetres of blood being injected into each buttock. The treatment is continued until all the scales have disappeared and the plaques show little or no induration. This usually takes about two weeks. No complications, except for occasional blistering from the ultra-violet therapy, have been observed. Of a series of 2,000 patients, 15 per cent have not had any return of the disease, 70 per cent have had remissions lasting from several months to many years, and 15 per cent have been relieved for only two or three months.

Treatment by lipotropic substances

The 'psoriatic diathesis'—Acting on the hypothesis that psoriasis is the cutaneous expression of a disturbance of lipid metabolism, P. Gross and Beatrice Kesten have treated a series of patients with lipotropic substances derived from foods. Coal-tar ointment has also been used locally. About forty patients with chronic psoriasis of varying degrees of severity are at present under treatment with either defatted wheat-germ or soya bean lecithin, and in most instances the response has been satisfactory. The question of what substance is responsible for the improvement observed cannot be answered at present. The only known component, common to soya bean lecithin and wheat-germ, is inositol. The soya bean product contains much choline, whereas wheat-germ is poor in this substance. Wheat-germ contains the complete vitamin B complex which the soya bean preparation lacks. Both preparations were found to be capable of reducing the serum cholesterol level when this was abnormally high. In three patients who were given soya bean lecithin the respective cholesterol values were: before treatment 800 milligrams, 388 milligrams and 400 milligrams per 100 cubic centimetres; after

treatment 225 milligrams, 190 milligrams and 215 milligrams respectively. Similar falls were observed in two patients treated with defatted wheat-germ. It does not appear that dietary deficiency alone can produce psoriasis. The authors' suggested explanation of the disease is that the 'psoriatic diathesis' is a constitutional disturbance, often hereditary, and that the appearance of the skin lesions may be precipitated by various agencies, including (1) factors aggravating the constitutional weakness, such as puberty, the menopause, acute or chronic infections and climatic changes; (2) increase of fat in the diet; (3) relative deficiency in some dietary factor or factors such as vitamins which are required for proper enzyme action. The constitutional anomaly underlying psoriasis may act through the endocrine glands, liver or pancreas. Vitamins and hormones are both intimately concerned in metabolic processes and the fact that administration of various vitamins and endocrine extracts has proved beneficial in psoriasis can best be explained along these lines. The patchy character of the skin lesions in psoriasis may be accounted for on the hypothesis that the difference between psoriatic and normal skin is a matter of difference of threshold depending on local conditions. Traumatic factors may play a part, and the tendency of psoriasis to affect the elbows and knees is perhaps due to the liability of these areas to such insults as stretching of the skin, mechanical injury and reduced supply of oxygen.

EDITORIAL COMMENTARY—Modern Views on Psoriasis

The desire to find a single specific cause for the common disorder of psoriasis provokes hopeful suggestions with regard to aetiology and treatment but such suggestions rarely stand the test of time or of general application. Changes in medical outlook and new discoveries in therapeutic fields have turned attention from internal and external infective agents, endocrine and hormonal influences in aetiology, to disturbances in fat metabolism, to obscure reactions to focal infection and to vitamin deficiencies (F. Reiss, 1938). Treatment along dietetic lines, by sulphonamides, by massive doses of one or other of the vitamins and by ultra-violet light has been explored. Claims made from particular investigations have not been substantiated upon general application although they may be relevant in certain cases. The suggestion has been revived that changes in fat metabolism are responsible for psoriasis (H. C. Semon, 1935), but it seems probable that when such changes occur they are not causative of the psoriasis but are associated symptoms of the general constitutional disturbance (Pulay).

The undoubted facts remain (1) that the tendency to psoriasis is one which is inherited; (2) that, in young people particularly, infective disorders such as the acute specific fevers, tonsillitis, and so on, readily provoke attacks of psoriasis and may influence its persistence; (3) that psoriasis appears commonly at times of major physiological or psychological change; (4) that variations in physical or mental well-being influence the behaviour of psoriasis when an individual is subject to that disorder. It is widely admitted that in the adult there is a relationship, and in many respects a similarity, between the behaviour of psoriasis and those ills which we call rheumatic (H. W. Barber, F. Hunt, G. L. K. Pringle and W. Yeoman, 1938; E. Hunt, 1932), it is also true that psoriasis is influenced by climatic factors and is generally less in evidence in summer and in warm, sunny climes, and it is rare in the negro (F. F. Hellier, 1940). It is true that psoriasis is very susceptible to psychological influences and is readily aggravated and extended by external irritation.

In the hands of the enthusiast a great variety of internal and external measures can be made to produce impressive results, and, in the last resort, rest in bed and shock therapy will rarely fail to give temporary relief in any hands. It is not surprising from this that considered dermatological opinion tends more and more to turn away from the conception of psoriasis as a morbid entity indicative of a single aetiological agent and to accept the view that it is a reaction comparable with other constitutional reactions and dependent upon an inherited disposition (G. M. MacKee and P. D. Foster, 1936). This is no new conception of disease and it is one we are unlikely to abandon whatever further scientific discoveries may hold the medical field from time to time. In asthma, dyspepsia, rheumatism, and a number of similar constitutional disorders, the physician has learnt to regard each case as an individual problem, and there is no reason why he should turn from psoriasis in despair instead of adopting the same approach. It would seem true that in assessing prognosis and treatment we must take into consideration the question of inheritance and the suitability or otherwise of the physical and psychological environment of each patient, including the employment and place of residence (R. M. B. MacKenna, 1936). The general and mental health of the patient should be overhauled. It is clear that any source of toxæmia, infective or metabolic, any focus of infection, any dietetic or metabolic or other departure from normal health should be corrected, since it may be the trigger which activates this reaction (R. Hallam, 1934).

It is only after this adequate assessment of, and approach to, the problem has been made that we can usefully proceed to local treatment, and if any success has been achieved in the former field this aspect of the problem will be relatively simple. A short period of rest and the use of an oxidizing agent as local application, if used effectively, will rapidly clear the eruption. The use of dithranol in Lassar's paste, not more than $\frac{1}{4}$ –2 grains to the ounce, is probably one of the most effective local treatments. In obstinate cases shock therapy of mild or of pyrexial type can be employed with advantage. It is probably unwise, except in very rare instances, to use either X-ray irradiation therapy locally or arsenic by mouth. After a patient has been

cleared of psoriasis the most important prophylactic measure is the maintenance of general and mental health. There is a large proportion of psoriatics in whom daily ultra-violet light irradiation of the whole body, in suberythema dosage, is of value in preventing relapses, either by reason of its general constitutional influence or as the result of its action on the skin, or on account of both (W. H. Goeckerman, 1931).

War conditions have not materially affected the problem of psoriasis. Upon occasion an acute exacerbation or the maintenance of a severe outbreak may be attributable to the environmental influence of war service. The embarrassment caused to a patient and to his colleagues may necessitate either his discharge from the Forces or a change of industrial employment.—JOHN T. INGRAM.

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PSYCHONEUROSES AND PSYCHOTHERAPY

See also B.E.M.P., Vol. X, p. 232.

Psychoneuroses

Aetiology

Association with ophthalmic disease—In order to determine the importance of the psychoneurotic element in ophthalmological practice C. A. Bahn has reviewed a series of 215 male and 185 female patients who consulted him for various complaints connected with the eye. He discovered that a psychoneurotic factor was present in about 75 per cent, as compared with about 50 per cent, the figure given by one authority, in general practice. The following causes are probably responsible for this high rate. (1) Efficient sight necessitates more elaborate coordination of automatic and voluntary neuromuscular mechanisms than does any other sense. (2) Visual function tests reveal automatic imbalance and fatigue reactions with greater accuracy than can be attained elsewhere in the body. (3) The eye is a peculiarly sensitive organ. Almost every ophthalmic symptom may have a psychoneurotic element. A detailed history must be taken in every case. Separate treatment of the functional and organic components is essential to success in every case. If optical, medical or surgical treatment is considered necessary it should be given promptly. For the psychoneurotic factor a 'health routine' is prescribed, covering the patient's whole twenty-four hours. The patient must be warned that improvement can be expected only if he adheres strictly to this regime.

Psychopathology

Psychoneuroses in recruits—A. T. Mathers, addressing the Royal College of Physicians and Surgeons of Canada, deals with the psychoneuroses in war-time. He tentatively defines psychoneurosis as a failure to achieve full happiness or usefulness because of uneasiness emanating from inward conflict. The whole personality is involved, and the predisposing cause is an inadequacy in the intangible part of the individual, sometimes inborn but more often acquired as a result of imitation or of defective education. Such vulnerable personalities should, as far as possible, be kept out of the Forces. Any sudden stress or strain, an illness or even suggestions of friends or of the doctor may be the precipitating cause. No distinctive war type of psychoneurosis occurs, but war itself carries with it an inevitable psychological tension which in the present war is being deliberately exploited. In regard to diagnosis, the importance of thorough physical examination cannot be overestimated. Treatment is an educational process and recovery is rarely uninterrupted, therefore much patience is needed. The cooperation of the patient is essential, and if chronic invalidism is to be avoided treatment must be given early.

Effort syndrome, emotion syndrome.—A paper read by C. H. Fitts at the annual meeting of the Royal Australasian College of Physicians dealt with the effort syndrome, for which he would substitute the term, emotion syndrome, using the latter to include functional dyspepsia and breathlessness on exertion. The latter syndrome is seldom seen nowadays, whereas functional dyspepsia has greatly increased. Fitts believes that suggestion caused by advertisements of antacid powders is largely responsible, and that similar suggestion directed towards the heart would probably induce the cardiac syndrome in emotionally unstable subjects. He quotes the case of a youth who developed cardiac symptoms a few days after being rejected for military service because of mitral stenosis, of which he had previously been unaware. It is unwise to draw patients' attention to disorders of the heart or stomach, or to submit a patient to repeated examinations. In a case known to the author, three barium meal investigations

were made within six months. The treatment of such patients is psychiatric. Specific remedies (digitalis, antacid powder) have no place. In the Army treatment is a front-line job for the regimental medical officer. Patients should not be sent into hospital unless it is absolutely necessary. In civil life it should be recognized that the problem is social rather than medical. Too many unstable personalities exist in our communities, and the cause is often to be found in an unsatisfactory family life.

Clinical picture and classification

Effects of air-raids on civilians.—In an endeavour to estimate the mental effects of war conditions, especially air-raids, upon the civil population, A. Lewis has collected evidence from various localities. He finds that there has not been any striking increase in neurotic illness, and some statistics even suggest a drop, but the available data are scanty and sometimes conflicting. Reports of increased local incidence were received from several sources. In Bristol, for example, the staff of the Child Guidance Clinic investigated fifty families who were spending the nights sleeping on the floor of a tunnel holding 3,000 people, and found that forty-one included one or more members suffering from neurotic illness; but as they point out, shelter populations are likely to contain an abnormally high proportion of nervous and unstable subjects. After intensive raids there is usually a slight rise in the numbers of cases of neurosis in the affected area, chiefly among those who have suffered from a neurotic illness before. The incidence among civil defence workers has been low. Children in general have not been much affected. The number of police-court cases of drunkenness has declined, although it must be borne in mind that populations have lessened and that the police may have been occupied in duties more important than the arresting of drunken people. Suicide has declined in Scotland, figures for England and Wales are not available. A considerable rise has taken place in road accidents and in juvenile delinquency. Insanity in general has not increased. The author points out that many causes of mental strain arise under war conditions, quite apart from air-raids.

Hysterical stupor treated by cardiazol.—W. L. Neustatter reports a case of hysterical stupor successfully treated with cardiazol (leptazol). The patient, a soldier, aged twenty-three, had been at home on leave, during which time he was said to have hit his head against a fence in the dark and to have complained of headache next day. On the day his leave expired he disappeared and in due course was posted as a deserter. Two months later he was picked up unconscious by the police within a few miles of home and was admitted to hospital. He was collapsed and stuporous, with a quick pulse and low blood pressure. The eyes were shut and he resisted attempts to open them. The only abnormal neurological sign elicited by examination was complete anaesthesia to pinprick and to heavy pressure. The blood Wassermann reaction was negative and the cerebrospinal fluid and a radiograph of the skull were normal. The urine obtained by catheterization contained acetone bodies. A month after admission he still lay inert, not making any response to tests requiring cooperation, but if left alone with food he ate it. Evidence of psychosis was not obtained. After an unsuccessful trial of hypnobarcosis, cardiazol (leptazol) therapy was instituted. After three convulsions during five days the patient sat up in bed and began to speak, and by the end of a week he had completely recovered. Questioning elicited that fear of bombing had led him to desert and was the cause of his hysteria. He was ultimately invalided from the Army on grounds of 'temperamental instability'.

Psychogenic illness in the Forces.—W. L. Jones describes forty-two cases of psychogenic illness in an army unit. They were classified as follows. anxiety state, nineteen; hysteria, twenty-one; psychosis, one; psychopathic personality, one. The station, a town in the south of England, did not experience any enemy action during the period under review. Conditions were good and the sick rate consistently low. The most frequently recurring symptom was headache, of which the site and character varied but which was always induced or aggravated by wearing the steel helmet. Defective vision was a prominent feature of six cases: the chief complaint was that print became blurred after a few minutes' reading and glasses did not improve matters. Effort syndrome occurred in seven patients. In five cases grosser manifestations of hysteria were observed. two men had convulsions with loss of consciousness; one had persistent pain in an operation scar and pseudo-epileptic attacks; one showed the effort syndrome and loss of consciousness; one presented the 'syndrome of approximate answers'. Each man was kept back after sick parade for physical and psychological investigation. In fifteen cases a sympathetic hearing, full examination and reassurance, sometimes with the addition of a change of conditions and a sedative, sufficed to keep the patient at duty. If after three or four interviews an improvement was not seen, the advice of the area psychiatrist was sought. Sometimes the man was placed in category C (home service only) or transferred to the Pioneer Corps. Nine patients were admitted to E.M.S. neurosis centres. One subsequently returned to duty, three were invalided, the remainder were lost sight of. Hysteria seemed to be the reaction of the man of subnormal intelligence to conditions too difficult or unpleasant for him. In the anxiety neuroses a morbid fear was the determining factor. It should be recognized that men may be physically fit but psychologically unfit for any form of military service.

Anxiety psychoneuroses

Association with cardiac disease.—F. A. Willius points out that worry plays an important part in cardiology, not only when heart disease is present but when it is not present although suspected. This is also true of all categories of disease. This frustrating reaction is an important

factor in both the development and perpetuation of various visceral neuroses. It is doubtful whether any person has entirely escaped worry. It is useless to tell an individual not to worry although the problems which comprise the basis for worry usually do not eventuate in realities. The trifles of life which for the time being loom with the magnification of twilight shadows occupy much attention, while actual impending calamities usually occupy only a small part of an individual's consideration. It is important to distinguish clearly between the act of worrying about a problem and being concerned about a problem. Worry, which is a protracted or recurrent act of the mind, follows devious and complex courses, always fails to result in a constructive solution of the problem and eventuates in confusion, fatigue and emotional instability. Concern on the other hand comprises interested and usually deliberate consideration of a problem in an orderly manner, with acceptance or rejection of apparent facts and contradictions. Concern ultimately results in an acceptable conclusion. Even although the latter may be contrary to the individual's wishes, it is accepted philosophically and for the very reason that a definite conclusion has been reached, the effort has been constructive, and confusion of thought has not resulted. Mental tranquillity, or peace of mind, is necessary for most individuals to be efficient and productive in their undertakings. But those to whom life consists of a series of recurrent and inexplicable complexities have insidiously developed a complex of insecurity in which even relatively unimportant decisions cannot be made readily. This group of persons, with few exceptions, comprises those who worry; their nervous reserve is squandered, they are perpetually tired. Man cannot escape from himself or his problems, although some attempt this impossible feat. This is the tragic procedure which leads to addiction to alcohol, narcotics and so forth.

Neurosis and the Army

Importance of individual morale.—According to J. R. Rees the Army has always contained a large proportion of the 'psychopathic tenth' of the population, men who were immature or unsatisfactory and who, it was thought, might do better under discipline than trying to support themselves as wage-earners. In peace-time this seems to work fairly well, but in war-time all sorts of problems arise. In active warfare some of these men might have given good service, but in conditions of inaction and monotony such as those which have been forced on many units in Great Britain they tend to break down. One of the main problems is that of individual morale. It has recently been decided to attempt to separate patients who are likely to return to the Army after treatment from those who will need rehabilitation and discharge, setting aside different hospitals for each type. Those who are likely to return to duty continue to receive some military instruction during their stay in hospital, so as to avoid needless waste of time. Men who are considered unfit for their former unit but fit to work in some special trade in the Army receive appropriate teaching; over 70 per cent have made good. Acute war neuroses brought on by active service have a good prognosis.

Occurrence of war neuroses

Importance of psychopathic disposition.—A Leading Article in the *Lancet* comments upon the way in which events have falsified pessimistic prophecies about the incidence of neuroses in war-time. In this respect the effect of air-raids has been almost negligible. In both civil and Service populations, however, the importance of the psychopathic disposition has been clearly revealed. For example, a London general practitioner during a period of severe air-raids found evidence of previous instability in three-quarters of the neurotic patients presenting themselves for treatment. Recovery or great improvement took place in only 25 per cent of the neurotically disposed, but in 70 per cent of the others. Evacuation seems to have been a good prophylactic against air-raid neurosis. Most of those who wished to leave the more exposed areas have been able to take advantage of Government schemes for evacuation, and those who remained behind have been on the whole the stable elements of the population. The soldier, on the other hand, cannot choose his post and, if it proves too much for him, cannot leave it. Many of the neuroses in Service patients have taken the form of attempts at escape from an intolerable situation, such as amnesic and fugue states, absence without leave and desertion. Worry and other stresses, such as breaking up of family life, have been prominent causes of neurosis. For the civilian, separation from the family has been at least in part voluntary, but for the soldier it has been compulsory. The degree of strain depends greatly upon whether an ordeal is voluntarily or compulsorily undergone, and many men who are fairly well adjusted to civil life but who are more than usually dependent upon their home environment break down quickly after entering the Army. Except in the hyperacute anxiety states, physical factors have not played a very important part in the production of neurotic illness. Owing to the successful management of our food supplies, defects of nutrition have not been conspicuous. Long-continued physical exertion and lack of food and sleep were largely responsible for the more severe cases seen after Dunkirk, and for similar syndromes which have occurred in shipwrecked seamen. Acute anxiety states have been rare among civilians in Great Britain, although *formes frustes* have been seen in people who owing to severe raids have had several sleepless nights; the condition was temporary, passing off with sleep and proper care. The advantages of deep shelters are the relief which they provide from the noise of an air-raid, the sense of security and the possibility of sound sleep. Special problems have arisen in connexion with the old and the young. The care of the old has become more than usually difficult, and increasing numbers have been obliged to enter institutions. A considerable rise has taken place in juvenile delinquency. The importance of a

stable family life has been vindicated. When this is unattainable some substitute must be provided to satisfy the emotional needs of the individual. For the man in the Forces his unit or his ship's company offers such a substitute.

War neurosis

Civilians and war injuries.—A study of the first 100 patients treated as in-patients at an E.M.S. neurosis centre has been undertaken by W. S. Maclay and J. Whitby. All these people were referred by the Ministry of Pensions because they had been receiving 'war injury' allowances for long periods. The comparatively low incidence of neurotic casualties is emphasized. Of the patients seventy were men, of whom twenty were in services such as the N.F.S. and the police, and thirty were women, none of whom were in these services. The average age was forty-five years, which is significantly higher than that of other patients attending practitioners at this period and indicates that the strain fell most heavily on older people. Thirteen had a previous history of neurosis, three of psychosis. Most of them had a good personality prior to the incident: 90 per cent of the men had steady work records. All the patients had been closely exposed to bombing, and eighty-six had endured severe mental stress. Fifty had received physical injuries. The average duration of incapacity before admission was seven months. The factors chiefly responsible were fear of another such experience (39 per cent); domestic and financial worries (42 per cent); pensions considerations (13 per cent); physical factors (24 per cent). Numerous other psychological considerations, often unrelated to the war, played a part in keeping up the illness. In most cases several factors were involved. The diagnosis was often mixed, but classified according to the most important symptoms most cases fell into the groups of anxiety state, hysteria and depression. The policy of in-patient treatment of psychiatric casualties was justified by the results. Most of the patients responded quickly and satisfactorily to treatment and 76 per cent were able to return to work of some kind. Subsequent observation of thirty-six of these patients showed that recovery or improvement was maintained for at least six months after leaving hospital.

Psychotherapy

General treatment

Acute war neuroses.—The value of drugs in the treatment of acute war neuroses is emphasized by W. Sargent, writing from experience gained in an E.M.S. neurological unit which has treated over 3,000 patients from the Forces alone. Such treatment can greatly expedite recovery and so enables the hospital beds to be used to the best advantage and patients to pass out quickly, fit either for modified Service life or for a civilian occupation. The supreme need is for adequate first-aid treatment of the acute neurosis occurring in a patient of previously stable personality; if the best results are to be obtained it is a matter of hours rather than of days. Sedatives in doses sufficient to produce some hours' unconsciousness, given at the first sign of breakdown, may prevent the development of a serious neurosis. Paraldehyde (2 to 4 drachms), sodium amylal (6 to 9 grains) or other sedative may be used, including, in an emergency, alcohol; but the best, because the quickest, is an intravenous injection of a barbiturate. In times of stress smaller prophylactic doses of sedatives may carry a man through, and stimulants, for example benzedrine, may also be of value to tide over a few hours of stress. Intravenous barbiturates are valuable also in cases in which there are hysterical conversion symptoms and which if left untreated for more than a few hours may become ingrained. If severe anxiety or hysterical symptoms have continued for a week or more, a much longer period (from seven to ten days) of continuous sleep treatment is necessary. The patient should be kept asleep for twenty hours out of the twenty-four, yet not so deeply asleep that he cannot be roused to take good meals. When the onset has been insidious with loss of weight, insulin therapy is often useful. Convulsion therapy gives good results in 75 per cent of cases of long-standing depression.

Reconstruction in psychiatry.—For his presidential address to the Section of Psychiatry of the Royal Society of Medicine, A. A. W. Petrie chose as his subject 'Reconstruction in Psychiatry'. At present psychiatry is viewed from different points by the academic psychologist, the medical psychologist and the industrial and educational psychologists, and closer cooperation between workers in different corners of the field is of great importance. Useful work is being done by such bodies as the National Council for Mental Hygiene in linking various psychiatric activities together. The physical and mental health services should be closely united, as they now are in London. Public bodies should establish mental health committees to deal with all questions relating to mental health in their areas. Problems of educational psychology, including child guidance, and of mental deficiency should be included in any scheme. Beds for mental and for psychoneurotic cases are best provided in special clinics serving a group of hospitals, including teaching hospitals. Mental hospitals will still be needed for chronic or irrecoverable cases of mental disease. Social services are designed to prevent or to diminish segregation, which is a large and costly problem. Recoverable patients who need treatment should be kept apart from patients who need only segregation. As a preventive measure, voluntary sterilization of abnormal people is recommended although it is of limited efficacy. Medical students should be taught to take into account the psychological qualities of every patient whom they see. Specialist training should be designed to produce the neuro-psychiatrist, who should have an expert knowledge of both organic and functional nervous diseases. Research scholarships should be provided. Spiritual guidance by

the priest may be of value for the disturbed but normal person, while the doctor alone should deal with the person who suffers from psychoneurotic symptoms.

Use of sodium amytal — L. I. Altman recounts experiences with sodium amytal as an aid to psychotherapy. Sodium amytal is a supplement to, not a substitute for, suitable investigation, explanation, suggestion and reassurance. Five cases of hysterical disabilities among soldiers have been treated, with complete relief in all. It was observed that these patients were very little affected by the dose of sodium amytal used (7½ grains intravenously). In all these cases strong suggestive psychotherapy was administered with the drug and none of the patients fell asleep. In a number of controls in which psychotherapy was omitted deep sleep ensued and the symptoms were not relieved.

Psychotherapeutic methods

Experimental observations — J. H. Masserman claims to have produced neuroses in cats. Each animal was trained to lift the lid of a box in response to a signal to secure food. When the cat had learned to do so, a blast of air was suddenly sent across the box while it was feeding. The cat soon began to show manifestations of anxiety whether it was in or out of the apparatus, with 'phobic' responses to the feeding signals and so forth. These symptoms persisted for months but could be diminished or abolished by the following procedures, which were most effective when used in combination: (1) Abolition of hunger by feeding the animal before it was placed in the situation of conflict. (2) Reassurance and persuasion. (3) Slowly pushing the animal into the box. The sight of the food eventually broke down its inhibitions. (4) Allowing the cat to witness the behaviour of a non-neurotic animal. (5) Allowing it to 'work through' its conflict by training it to manipulate the switch which controlled the feeding signal and the automatic deposition of food in the box. By such treatment most animals regained confidence. The results of the experiments are held to confirm the value in neurosis in human beings of a combination of similar psychiatric procedures, namely initial relief of anxiety, establishment of confidence in the psychiatrist, the employment of personal relationships to induce the patient to improve his social conduct, graded pressure on the patient to force him to solve his emotional problems and the provision of vocational or other means to enable the patient to work through his maladjustments.

EDITORIAL COMMENTARY—Neurosis and the War

Psychological medicine in Great Britain, with a high proportion of its specialist practitioners in the fighting services, and with many of those who remain in civil life interested in the auxiliary services, has recently been almost exclusively concerned with problems arising out of the war.

A survey of the incidence of psychoneuroses under war conditions (A. Lewis, 1942) has confirmed previous observations (R. D. Gillespie, 1942) that the present war has produced a very small increase in their prevalence among civilians. Some statistics from a general practice suggest a slight increase, especially in those who had had a neurotic illness previously (Lewis). The prognosis of psychoneurosis attributable to air-raid experiences is as a rule good. Most such reactions are very transient. Thus, of 134 civil patients, all left hospital within twenty-four hours and only six are known to have required further treatment (H. Wilson, 1942). But previous statistics have suggested that there might be delayed after-effects of a more chronic kind.

All writers seem to be agreed on the importance of predisposition in psychoneurosis arising out of the war, whether in members of the Forces or in civilians. The proportion found varies in accordance with differences in the standards adopted by the observers and in their opportunities, and more especially in accordance with the kind of material observed. Thus, in a psychiatric hospital in Great Britain with troops under training conditions predisposition has been described in 82 per cent (J. A. Hadfield, 1942), while among Australian troops at Tobruk, 35·2 per cent were regarded as having had some kind of predisposition (H. R. Love, 1942). In sixty-three Civil Defence workers with 'subacute' psychological symptoms after an air-raid 48 per cent were found to be considerably predisposed (Wilson). The predisposition described is usually in the family history, or a history of 'nervous breakdowns', of previous neurotic symptoms, and of chronic physical complaints for which a definite organic cause has not been found, or of frequent changes of job, but there are many other factors to be taken into account, such as over-dependence on home, including some that require time and special experience to elicit. These observations reinforce the view that psychiatric selection, if it can be done adequately, should be of great value, both as a preventive of psychoneurotic and other forms of psychological breakdown, and as a means of increasing the efficiency of any Service, either by rejecting the unstable or placing them in jobs familiar to them from civilian experience or suited to their aptitudes. The armed Forces now submit all their recruits to a group intelligence test, rejecting individuals with the lowest score only after a psychiatric examination to confirm the value of the group score, and to ascertain the man's or woman's actual employment history and other facts bearing upon stability of temperament and predisposition generally. This method does not pick out the majority of the potential psychiatric casualties, but it eliminates a proportion of them, and it allows the dull man to be allotted to duties within his capacity, for example in the Army to the armed or unarmed pioneers, according to his degree of dullness of intelligence. The same principle in a different form can be applied to the upper end of the scale, in the selection of officers, but the relevance

to fighting capacity has still to be demonstrated in the experiences of the battlefield (J. R. Rees, 1943).

As regards treatment, the war has brought home an old truth—the value of rest in the treatment of many psychiatric casualties. Mild depressions, especially in people of obsessional temperament, anxiety states whether in fighting men or Civil Defence workers or industrial employees who have long worked overtime, will often clear up with a few weeks' good well arranged rest, and little else. It is worth remembering that war is more productive of fatigue in most people than is peace because of the spurts of special effort, which is more characteristic of the fighting man, and which, because of the long continuous overwork, is apt to be the lot of some civilians. Nine-tenths of the psychiatric battle casualties in the Middle East, according to Craigie, turned out to be states of exhaustion which, with about forty-eight hours' rest, aided by sedatives if need be, were restored to normal. It is quite likely, however, that as doctors we have often overlooked the share of the same factor in producing psychoneurotic forms of illness in peace-time, not only in the poorer, but also in the middle classes, especially with regard to the mothers.

In the more severe psychological upsets more drastic methods are applicable. Panic indicates the use of a sedative sufficient to produce sleep for the greater part of twenty-four hours. Paraldehyde—four drachms; sodium amytal, 3 to 6 grains; nembutal 3–4½ grains by mouth—all of them capable of repetition to some degree after four or six hours—are recommended, not only with the object of relieving symptoms of acute panic, but also in the hope of preventing the development of a chronic state of anxiety (W. Sargant, 1942). It is possible that emergency treatment of this sort may have some prophylactic value by limiting the impressions made by the disturbing event—partly by preventing ruminations and partly by a more direct physiological effect. The intravenous route may be used in the barbiturates, and the result is produced more quickly. When chronic anxiety symptoms of a severe degree persist, continuous narcosis has been recommended, but this can be carried out only in a hospital with a specially trained staff, as the treatment is not without risk. For individuals of good material who have broken down under severe stress, with loss of weight, an insulin fattening technique has been used (Sargant), but while it helps the patients physically and also gives them encouragement it does not seem to make them able to return to active service in any greater proportion than does a well planned rest period.

In the psychiatric forms of illness the main interest has continued to be in shock therapy. The electrical method is now the only form of shock therapy being used, because of the advantages both to the patient's comfort and safety and to the administrator. It is effective in nearly every case of involutional melancholia in which it is tried, and in most cases of simple severe depression in younger patients. Its drastic and rapid effect, however, has caused some misuse. It is no light matter to inflict brain damage, however temporary, especially on a young person's brain, this method is sometimes applied in cases in which even a little patience would produce a happy result. It has also been applied to a miscellany of other conditions with little justification and as a forlorn hope. The results of shock treatment are not nearly as good in schizophrenics. Even when improvement is produced relapse is common. Insulin coma is to be preferred here. When both fail leucotomy (cutting the white matter in both frontal lobes on either side of the midline and thereby probably severing the fronto-thalamic tract) in certain cases is justifiable (J. S. McGregor and J. R. Crumlie, 1942). This method, or something like it, has come to stay in the alleviation or apparent cure of chronically disturbed and violent schizophrenics, and possibly also in cases of chronic depressions, especially those with obsessional features. In favourable cases recovery begins almost as soon as the operation is completed, and complications although they can be severe or even fatal are uncommon. There may be little definite departure from normality in the patient subsequently, and some authors have even observed that the patient's personality is improved. It has been stated that although apparently normal the treated patient suffers from some inability to use the memory of past experience, and so lives on a rather superficial level of current associations (E. L. Hutton, 1942). A blunting of emotional responsiveness has also been noted.

—R. D. GILLESPIE

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PSYCHOPATHIC PERSONALITY

See also B.E.M.P., Vol. X, p. 260.

Clinical picture

Predominantly passive or inadequate type

Medico-legal aspects of delinquency.—D. Kerr, in his Honyman Gillespie lecture, deals with the problem of delinquency in its relation to Medicine and particularly with the procedure adopted in the Edinburgh courts. Although delinquency in itself is not of itself evidence of disease or mental abnormality, a small proportion (about 4 per cent) of delinquents are mentally ill or abnormal and are in need of medical attention. The first problem before a court is the detection of such cases. The evidence may suggest that a mental factor is present, but many abnormalities will escape a layman's notice. Routine psychological examination of delinquents is impracticable, but certain offences are so often associated with mental abnormality that they call for preliminary investigation from that standpoint. In Edinburgh selected persons are thus picked out for preliminary medical examination. Scottish law recognizes a condition of diminished responsibility, not amounting to insanity, which may be taken into consideration in sentencing an offender. Some acts which are misdemeanours in English law are not offences in Scottish law, for instance, attempted suicide, which in Scotland is an offence only if it can be considered a breach of the peace. In Edinburgh many such delinquents never appear before a court. One of the most valuable results of medical investigation of delinquents is the prevention of further delinquency by bringing the individual under the care of the social services attached to the court. In many cases adjustments can be made between the delinquent and his surroundings. The main causal factors, in juvenile delinquency at least, are environmental.

Neurogenic fever

Neurosis, recurrent pyrexia and migraine. S. Wolf and H. G. Wolff discuss the nature of 'neurogenic fever' which has never been defined accurately, and record the case of a man, aged forty-three, with a history of neurosis and recurrent attacks of fever (104° F.) and migraine for thirteen years. The patient was exhaustively examined, and a personality study uncovered a great many personality disorders. He was then free from the bouts of fever and migraine for a year; a further period of anxiety tension was however succeeded by a relapse of fever. The mechanism responsible for the febrile attacks is not clear, but it is suggested that the attacks may be due to a vasomotor disorder like that responsible for migraine.

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PSYCHOSES: AFFECTIVE PSYCHOSES

See also B.E.M.P., Vol. X, p. 267, and Cumulative Supplement, Key No. 1319.

Aetiology

Factor of hostility

In manic-depressive psychosis—The role of hostility in the causation of affective psychoses has been studied by Jane E. Oltman and S. Friedman. They find that the presence of hostility, a sadism which tends to destroy completely the love object, is a feature of both phases of the manic-depressive psychosis. The depressed patient does not give open expression to his hostility and hatred, and often goes to great lengths to disguise them. In many cases he uses the mechanism of projection to transfer his emotions to others, and expresses a belief that he is hated by other people. The depression is a guilt reaction. During the manic episodes the patient openly expresses hostility to members of his family. In female patients it is usually directed against the husband. It is probable that the hostility of patients with affective psychoses springs from an original focus of hostility and ambivalence towards one or more of the family circle. The reason why a depressed patient conceals while a manic patient reveals his emotions is found in the stronger, more rigid superego of the depressed patient. The manic patient is satisfied with himself and critical of others, and his weaker superego permits full expression of his hostile tendencies.

Treatment

Specific

Curare in convulsion therapy.—J. A. Cummins reports the results of the use, since December, 1940 at the Ontario Hospital, Hamilton, of a preliminary dose of curare in 118 patients with psychogenic psychoses, especially of the manic-depressive type, in order to minimize the incidence of compression fractures of the vertebrae. Curare acts on the neuromuscular mechanism by interrupting transmission of the nervous impulse as a result of neutralization of acetylcholine, the essential neuromuscular stimulating factor. The margin between the treatment dose and the dose causing paralysis of the respiratory muscles is small. One milligram ($\frac{1}{16}$ grain) of active curare per two pounds of body weight is a safe and adequate dose.

Curare first paralyses the skeletal muscles and lastly the diaphragm and intercostal muscles; it is given intravenously slowly for a minute and then a period of two or three minutes is allowed, so that the effect of the curare may develop, before the injection of metrazol (leptazol) is given. For sudden paralysis of the muscles of the neck, the ideal remedy is the intravenous injection of 2 cubic centimetres of prostigmin (neostigmine); this unites with curare, and frees acetylcholine which plays a part in the transmission of nervous impulses; artificial respiration has been employed but is less effective. The author concludes that metrazol combined with curare is a relatively spectacular remedy and strikingly reduces the seriousness and incidence of fractures—from 14.8 to 3.4 per cent. There is not any evidence that curare in any way diminishes the therapeutic power of metrazol. In two patients preliminary radiological examination showed generalized osteoporosis, and therefore metrazol treatment was not adopted.

Endocrines in involutional psychoses—E. Davidoff and G. L. Goodstone have administered an androgen preparation (testosterone propionate) intramuscularly to twenty male patients with involutional psychosis. The dosage was as follows: first week, 10 milligrams daily to fifteen patients and 25 milligrams three times a week to five patients; next four weeks, 30 to 50 milligrams a week; when sufficient improvement was not obtained, a weekly dose of from 20 to 25 milligrams or, in six cases, from 50 to 75 milligrams, was given for another four weeks. The average duration of treatment was six weeks. Fifteen patients have been observed subsequently for over a year. The psychoses were of mild, moderate and severe types. Thirteen of the patients improved under treatment—a larger proportion than that observed in a series of patients treated without the androgen. The mild and moderate types responded best, the severe type hardly at all. Untoward effects, mostly temporary, were observed in all the patients; the most common were 'general cutaneous and vasomotor manifestations' and headache. Three of the patients became increasingly depressed, and two attempted to commit suicide. The therapeutic test with testosterone propionate is suggested as a possible method of differentiating between involutional psychoses in which androgenic deficiency is an important aetiological factor, and the more severe types in which other factors predominate.

Involutional melancholia with hypopituitarism.—R. E. Hemphill and M. Reiss describe a special form of involutional melancholia in which hypopituitarism and secondary hypoadrenalism are factors. Nine such patients (three males, six females) were treated by a purified extract of corticotrophic hormone free from growth, gonadotrophic and thyrotrophic fractions, given intramuscularly in sudanophobic units. In addition to the nine cases two other patients with Simmonds's syndrome were treated in the same way. In the patients the thyroid gland was small or impalpable, and the breasts and external genital organs were stunted. The urinary excretion of 17-ketosteroid was subnormal, a common change in hypo-adrenalism and in hypopituitarism. As a result of the treatment there was improvement, both physical and mental.

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PSYCHOSES: SCHIZOPHRENIA

See also B.E.M.P., Vol. X, p. 302; and Cumulative Supplement, Key No. 1321.

Clinical picture

Mental symptoms and signs

Emotional immaturity and regression.—A comparative study of the emotional maturity of schizophrenics and manic-depressives leads M. A. Durea to certain conclusions. The average emotional age, as estimated by Pressey's 'interest-attitude' test, is lower in both the above types of patient than in a normal control group, and the difference is greater in the schizophrenics than in the manic-depressives. The mean emotional ages for the three groups were 20.5 (control), 15.5 (schizophrenic) and 16.5 (manic-depressive). As compared with the control group the schizophrenics are most retarded emotionally by test II (worries), the manic-depressives by test IV (admiration). Emotional regression seems to be an integral part of the schizophrenic syndrome; the manic-depressive state is not characterized by emotional deterioration.

Onset, course and treatment.—R. A. Noble points out (1) that schizophrenia is the morbid exaggeration of a mental reaction which is present to a greater or less extent in everyone, and (2) that heredity is an important factor in the aetiology, about which otherwise little is known. The onset may coincide with a period of rapid growth; it is usually insidious although it is sometimes acute, especially after an illness, and prodromal symptoms are generally present. The usual picture is that of an adolescent who becomes progressively more retiring, dreamy and preoccupied; when roused from day-dreaming he may make an eccentric reply; sometimes a meaningless sentence is inserted in a letter. Affect is distorted, usually becoming shallow. Hallucinations may be visual or auditory but are generally of the latter type, and delusions are often non-systematized and fleeting. The course of the illness varies. Generally a period of abnormal conduct is followed by apathy which often progresses to dementia, but

the illness may be arrested at almost any stage and the patient, although perhaps he still shows some oddity, may be able to return to ordinary life. Recovery takes place in 30 per cent or more of the patients. The more sudden the onset and the greater the previous mental or physical stress, the better the prognosis. Successful treatment depends upon early diagnosis. Institutional treatment is often advisable. Insomnia must be treated and the general health should be attended to. Special treatment consists in shock therapy. Repeated induction of hypoglycaemia has been superseded by convulsion therapy; this was at first carried out by injection of cardiazol (leptazol), but the electric shock method now widely in use avoids any discomfort to the patient and seldom causes unpleasant sequelae; it requires special care in administration and the apparatus costs about £50. Surgical treatment (prefrontal leucotomy) has been tried in a few cases, apparently with some success.

Catatonic

The catatonic pupil.—A. Levine and P. Schilder have studied the mechanism of the catatonic pupil in a series of twenty-one patients of whom six showed this phenomenon, which is characterized by inequality in size and variability in the response to light. The reactivity of the same pupil changes from minute to minute. It is common in although not confined to psychotic conditions. Latent defects can sometimes be brought out by using Redlich's or Meyer's procedure (active muscular exertion and passive pressure respectively) or by emotional stimuli. In the authors' observations the pupillary reactions were impaired by instillation of different drugs, and their findings were as follows. After homatropine sulphate $\frac{1}{2}$ to 2 per cent had been used, Redlich's sign could be elicited up to the point at which abolition of the light reflex occurred; it appeared again in the restitution stage, the Meyer sign rarely could be elicited. Eserine (physostigmine) $\frac{1}{4}$ to 2 per cent and cocaine gave the same results. It was noted that drugs producing parasympathetic paralysis caused greater dilatation than sympathetic stimulants. Acetylcholine and mechoyl (acetyl- β -methylcholine chloride) had no effect upon the pupils. Changes slightly resembling those of the catatonic pupil are produced by anoxaemia due to inhalation of nitrous oxide, and injections of eithyoidine produce similar, more pronounced changes. The theory is advanced that the catatonic pupil is due to incipient inhibition of the parasympathetic system with consequent sympathetic-parasympathetic imbalance, and represents an intermediate stage on the way to complete fixation of the pupil.

Treatment

Specific

Insulin therapy.—R. A. Sandison and J. S. McGregor have used insulin intravenously for inducing hypoglycaemia in the treatment of schizophrenia in thirty-three patients, to whom 1,518 individual treatments were given over a period of one year. The chief advantage of the intravenous route in present day conditions is the saving in insulin; the initial dose is lower, and sensitization is produced more rapidly so that subsequent hypoglycaemic attacks can be induced by progressively smaller doses. The disadvantages of intramuscular insulin—delayed recovery, vomiting and late shock—are obviated by the use of intravenous insulin and by giving intravenous glucose, instead of sugar by a nasal tube, to restore consciousness; sugar is also saved by the latter practice. Vomiting occurred in a few patients who were given electrical shock therapy combined with coma induced by intravenous insulin. Hypoglycaemia develops earlier and more abruptly and is more profound with intravenous than with intramuscular insulin, and the therapeutic effect is therefore possibly more powerful. Fits during the period of coma are commoner when intravenous insulin is given. The fall in blood sugar is not maintained, the level returning to normal within an hour, in a number of cases intramuscular insulin was given as well, in order to keep the patient in coma longer; the results were not any better. Protamine zinc insulin was tried intravenously but did not seem to possess any advantages over ordinary insulin. The *modus operandi* of insulin is still unknown; it is suggested that in schizophrenia the autonomic centres are depressed and that insulin acts as a stimulant.

Shock therapy under review.—N. D. C. Lewis, Professor of Psychiatry, College of Physicians and Surgeons, Columbia University, discusses the difficult task of assessing the present position. For the past five or six years the pharmacological shock treatments have dominated psychiatric research with their main focus on schizophrenic disorders. During 1941 and up to 21st October, 1942 when this lecture was delivered, some 457 articles on the action of insulin, metrazol, electric currents and other shock producers, had appeared in scientific publications. Of these, fifty dealt with the effects of the convulsant metrazol (leptazol), forty-eight with electro-shock methods, sixteen with insulin and forty-three with other coma-producing drugs and procedures (nitrogen, sodium amytal and so forth). The published results present discordant opinions, and there is not any consensus on the basic value of the treatment; some are enthusiastic, others frankly depressing. The one thing certain is that shock treatment is receiving a very extensive clinical trial. There is a sufficient amount of scepticism to ensure a careful investigation and testing of the various problems and questions such as the following: (1) Will shock treatment finally go the way of many or not most other 'cures'? (2) Is the treatment specific? Does this radical approach offer a lasting benefit? (3) Is the treatment being applied improperly, inadequately or dangerously by many hospital staffs and private practitioners? (4) Does it help the patient to understand his personal problems, and does it help the psychiatrist to understand the patient, his disorder, his problems or his constitutional equipment? (5) Does it tend to discourage organized beneficial psychotherapy in general and to encourage neglect of the same in individual patients in particular? (6) Which type of shock

therapy is the most efficient and in what circumstances and for what disorders is a special therapy selected? Is electrical shock the most efficient in certain disorders or is its growing popularity based on its relative simplicity of application and its inexpensive features as compared, for example, with insulin? (7) Does the danger of damage to the body structure and to the brain in particular, outweigh any benefits that might be obtained from any of these treatments? Although as yet there is not any satisfactory answer to many of these questions some comments regarding them, based on reports, experiences and experiments are in order. Discordant results in scientific work indicate further investigation. As regards indications for treatment, some believe that in order to test soundly, the patients selected should be those with a hopeless prognosis. Stress is laid on the realization that all our classifications of knowledge, including those of mental disorder, are constructed by man out of his impressions and not necessarily made so by nature, and so may not be valid. There is not any distinction in nature between 'organic' and 'functional'. A table showing a comparison of the results of treatment by insulin, metrazol and electro-shock is given and shows a certain consensus of opinion in favour of insulin for schizophrenia, and of the convulsants, metrazol and electric current for involutional and other depressants including those in the manic-depressive syndrome. Many workers prefer combinations of insulin and metrazol and of insulin and electro-shock. In conclusion Lewis says he regards insulin, metrazol and electro-shock with the adjuncts recommended by some workers, and particularly when supplemented by systematic psychotherapy and other measures available in psychiatric clinics, as valuable in proper hands. But in some cases they have been misused. They are not a panacea for all mental disorders. At present there is not any sufficiently comprehensive theory regarding the nature of the shock reactions. Electrically induced convulsion therapy appears to be a safe and convenient method of treatment. So far there is not any reason to emphasize any particular contraindication to electrical shock which does not exist already in any other form of shock treatment.

Convulsion therapy by ammonium chloride.—K. N. H. Rizvi describes the use in thirty-nine schizophrenics (twenty-nine males, ten females) of 10 cubic centimetres of a freshly prepared 5 per cent solution of ammonium chloride injected intravenously. This method of inducing mild convulsions is less likely to cause fractures or cerebral haemorrhage than is the use of cardiazol (leptazol) and is far more economical. If the solution of ammonium chloride is not made on the day on which it is to be injected the salt decomposes and no effect is produced. There are three stages in the convulsive fit: (1) pre-convulsive, (2) convulsive and (3) post-convulsive or recovery. In about five seconds after the drug is injected the patient gets red in the face, but there is not a cough as there usually is with leptazol. The fit is very mild and lasts from fifteen to twenty seconds, the tongue is not bitten and there is not any cyanosis. Consciousness is usually regained before the muscular movements have ceased. Out of the twenty-nine male patients eleven were cured, eight were improved and ten were not improved; of the ten females four were cured, two were improved and four were not improved. Altogether, among the thirty-nine patients, 35 per cent were cured, 25 per cent were improved and 40 per cent were not improved.

Death after convulsion therapy.—Death of a patient with schizophrenia during treatment by metrazol (leptazol) and curare is described by G. L. Charlton, W. C. Brinegar and O. R. Holloway. The patient was a healthy man, aged twenty, with a two months' history of mental disturbance. It was decided to institute metrazol (leptazol) therapy with preliminary injection of curare to modify the convulsions and thus to prevent possible injuries. Four cubic centimetres of Intocostin, a preparation of which 1 cubic centimetre is equivalent to 20 milligrams ($\frac{1}{2}$ gram) of crude curare, were given intravenously during a period of slightly over one minute. After one and a half minutes ptosis developed, denoting partial muscular paralysis, and 5 cubic centimetres of a 10 per cent solution of metrazol was then rapidly injected into the vein. A convulsion occurred, at the end of which the patient died. Necropsy findings were negative, and death was thought to be due to the action of curare on the respiratory centre. The authors recommend that prostigmin (neostigmine) should be at hand whenever curare is used.

Spinal anaesthesia in convulsion therapy.—Against the undoubted benefits of electrical shock therapy must be set the possibility of fractures. To reduce this danger spinal anaesthesia is advocated by H. J. Shorvon and L. M. Shorvon for all patients aged under twenty or over fifty, or in whom any pathological condition of bone is demonstrated by X-ray examination. Four cases are reported in which stovaine (amylcaine hydrochloride) was given before the convulsion was induced. One patient had a tuberculous hip joint, another had a crush fracture of the spine, a third fractured the acetabulum during his first induced convulsion; in the fourth arteriosclerosis was present and the possibility of a vascular catastrophe was feared. Stovaine injections did not cause any ill effects, even when from three to seven injections were given.

'Sadistic therapy'.—H. Selinski contributes a paper on the present status of shock therapy of mental disorder. Selinski prefaces his paper by the emphatic declaration that he does not approve of the indiscriminate use of electro-shock. Without doubt it carries some risk, which varies with the judgment, experience and discretion of the medical practitioner. He mentions that as a therapeutic method it has provoked repugnance in the minds of many psychiatrists because of its apparent violence; some have referred to it as 'sadistic therapy'. On the other hand it has saved lives that otherwise would have terminated in suicide, and often has enabled a patient to carry on the work necessary to his livelihood without the serious interruption of going to an institution. He also insists that, like any shock treatment, it is

most incomplete if there is not also adequate psychotherapy. The author used a Rahm apparatus and the current was applied for 0.1 second, varying from 70 to 120 volts; a *grand mal* convulsion was aimed at generally, for increasing experience showed that it was most effective. The benefits due to electro-shock therapy are physiological and psychological. Selinski attaches more importance to the latter. He considers that the improvement which occurs is made possible by psycho-physiological alterations involving feeling tone.

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Durea, M. A. (1942) *J. nerv. ment. Dis.*, **96**, 663.

Levine, A., and Schilder, P. (1942) *J. nerv. ment. Dis.*, **96**, 1.

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Noble, R. A. (1942) *Practitioner*, **149**, 14.

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Sandison, R. A., and McGregor, J. S. (1942) *J. ment. Sci.*, **88**, 387.

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PSYCHOSES: TOXIC INFECTIVE PSYCHOSES

See also B.E.M.P., Vol. X, p. 316, and Cumulative Supplement, Key No. 1322.

Clinical picture

Variations from classical delirium

Bromide intoxication.—H. K. Detweiler reports six cases and quotes other examples of bromide intoxication from the Western Hospital, Toronto, the Henry Phipps Psychiatric Clinic in Philadelphia, and the Colorado Psychopathic Hospital. This toxic psychosis due to bromides was described as 'bromism' in 1868 by J. R. Reynolds after it had been in vogue since 1857, but this account of bromism had been forgotten until recently. Detweiler stated that there was not any pathognomonic sign or symptom of bromide intoxication but pointed out that it was specially prone to occur in chronic alcoholism and in arteriosclerosis, particularly of the cerebral arteries. Fortunately the administration of sodium chloride facilitates the excretion from the body of bromides. Medical practitioners should help the prevention of bromide intoxication by endorsing their prescriptions for bromide by the legend 'Not to be repeated'.

Detweiler, H. K. (1943) *Canad. med. Ass. J.*, **48**, 309

Reynolds, J. R. (1868) *Practitioner*, **1**, 5.

PSYCHOSES: PRE-SENILE AND SENILE PSYCHOSES

See also B.E.M.P., Vol. X, p. 342; and Cumulative Supplement, Key No. 1324.

Senile psychoses

Clinical picture

Symptomatology, diagnosis and treatment.—D. K. Henderson discusses senile mental disorders especially from the point of view of early diagnosis, suggesting that intensive study of the pre-psychotic characteristics of an individual may reveal an underlying diathesis, recognition of which may enable prophylactic treatment to be undertaken. Hereditary predisposition is common. Cases may be classified as diffuse senile dementia, focal atrophy of the brain or senile delirium. The symptomatology of all these types is extremely varied and may involve character, affect and intelligence. Changes in affect are to be regarded as being secondary to changes in character or intelligence. In most patients the earliest symptoms involve the intellectual functions and comprise easy fatigability, failure of attention and concentration and a tendency to repetition; a detailed investigation usually discloses increasing conservatism in ideas and habits. A secondary change of affect usually results in irritability, depression or suspicion and sometimes later causes delusions. Disturbance of memory is characteristic. Such symptoms occurring in combination suffice for diagnosis. In some patients character changes occur at the onset and may assume various forms. Senile mental disorders are distinguished from arteriosclerotic psychoses by (1) the higher average age in senile cases; (2) the mode of onset, which in senile cases is almost always gradual, and in arteriosclerotic cases is acute; and (3) the predominance of physical symptoms such as headache and dizziness in incipient cerebral arteriosclerosis, changes in personality coming comparatively late. As regards prophylaxis, people who are approaching the senile period should be taught to live within their limitations and to grow old wisely. Simple measures to improve general health, especially by administration of vitamins B and C, may do good. Superfluous drugging is to be avoided especially for the sleeplessness which is often troublesome.

Henderson, D. K. (1942) *Practitioner*, **149**, 1.

PSYCHOSES: GENERAL

Treatment

General

In general hospitals.—J. Weinberg and H. H. Goldstein review the statistics relating to the

treatment of psychotic patients in general hospitals in Chicago. The introduction of modern methods of treatment has resulted in an increased tendency to treat such patients in ordinary hospitals rather than to relegate them to asylums for the insane. General hospital treatment is acceptable to relatives; it removes the stigmata of the asylum and being limited in probable duration is likely to be within the financial capacity of the patient's friends. It lightens the burden upon the State of caring for the insane. Of sixty Chicago hospitals and sanatoria from which replies were received, twenty had admitted a total of 1,598 psychotic patients for treatment during 1940. The same group of hospitals during 1935 admitted 582 patients, that is the number of admissions had trebled. Seventeen of the hospitals which replied stated that some form of modern treatment, for example convulsion therapy or prolonged narcosis, was used for their patients. The result of the increasing tendency to treat psychotic patients in general hospitals has been a drop in the numbers of good results of modern treatment reported by the mental hospitals, which now tend to receive a larger proportion of severe and intractable cases, including the failures from the general hospitals.

Refrigeration

Failure of treatment.—D. Goldman and M. Murray report the results of refrigeration treatment in sixteen patients suffering from psychoses which had proved refractory to ordinary methods. The patient's temperature was maintained at a low level (82° to 86° F.) by means of ice packs for periods of up to 120 hours. No mental improvement was apparent in any of the patients. The chief complications encountered were (1) skin injuries from freezing and (2) respiratory infections. In only one case were skin lesions severe, but the respiratory complications, bronchitis or broncho-pneumonia, which occurred in five cases, were responsible for two deaths. The writers have abandoned the treatment somewhat disappointedly.

Specific

Electrical convulsion therapy.—R. E. Hemphill reports on a series of 200 patients (sixty-three males and 137 females) who were treated for various mental disorders by electrical convulsion therapy. Preliminary stimulation of the labyrinth by syringing the ear with cold water was always practised because it seems to facilitate the return of breathing after the fit. The instrument used was graduated up to 150 volts and, for time, in intervals of 0.05 second. The adequate shock for most patients was 150 volts for 0.3 second. Three methods have been tried, namely the induction of two fits weekly, three fits weekly and daily fits for two or more weeks. In each case treatment was terminated gradually by continuing three or four fits at weekly intervals. If after the ninth fit, improvement has not taken place the treatment is discontinued; recoverable patients usually show improvement before the fifth fit. Three patients sustained fracture of a bone during a fit; two apparently healthy patients developed active pulmonary tuberculosis, probably as the result of breaking down of fibrous barriers by violent movements, and both died within six months, one patient developed tuberculous adenitis of the neck; two had persistent cardiac arrhythmia after treatment which was therefore discontinued. The recovery rate for the whole series was 29.5 per cent. Of the schizophrenic patients (114) only four showed full remission, of sixty-four patients with affective psychoses forty-nine were discharged as recovered. Symptoms, however, may return if provoking factors are not removed, and shock treatment should be combined with psychotherapy. Improvement took place in 26 per cent of the patients in the series.

Goldman, D., and Murray, M. (1943) *J. nerv. ment. Dis.*, **97**, 152.

Hemphill, R. E. (1942) *Lancet*, **2**, 152.

Weinberg, J., and Goldstein, H. H. (1943) *J. nerv. ment. Dis.*, **97**, 40.

PUBLIC HEALTH

Vital statistics

Foetal mortality

Causal factors. D. A. D'Esopo and A. A. Marchetti have reviewed 1,000 foetal deaths occurring among 25,823 deliveries, with a view to determining the causes; necropsy was performed in 893 cases. Multiple factors were often apparent in a single case, and to assess their relative importance was often difficult. The gross foetal mortality rate was 4.03 per cent but, if only viable infants are included, it falls to 3.66 per cent. The premature infants are divided into pre-viable (twenty-second to twenty-eighth week) and viable (twenty-ninth to end of thirty-seventh week); among the former the mortality is nearly 100 per cent, but one pre-viable infant occasionally lives. Asphyxia (19.8 per cent) and prematurity (18.5 per cent) were found to be the commonest causes of death. The mother's age is of some importance; women over thirty have proportionately more dead babies than do women below that age. Maternal disease accounted directly for 6.3 per cent of foetal deaths, and indirectly (by leading to premature onset of labour) for another 5.5 per cent. The influence of the duration of labour is shown by the higher mortality rates for labours lasting under three and over thirty hours. As to the method of delivery, the mortality rates were as follows: in spontaneous vertex deliveries 2.6 per cent, in low forceps 3.3 per cent, in Caesarean section 7.3 per cent, in breech deliveries 14 per cent and in high forceps 41.4 per cent. Birth injuries accounted for a large proportion of still-births in cases of instrumental delivery; in the entire series they were responsible for 11.5 per cent of foetal deaths. Pelvic disproportion and bad mechanics in the use of forceps account for the majority of birth injuries. Improvement in ante-partum

care, obstetric training and care of the new born is necessary if foetal mortality is to be reduced.

D'Esopo, D. A., and Marchetti, A. A. (1942) *Amer. J. Obstet. Gynec.*, **44**, 1.

PUERPERIUM

See also B.E.M.P., Vol. X, p. 365; and Cumulative Supplement, Key Nos. 1326-1329.

Management of the normal puerperium

After-pains

Mechanical recording of muscular contractions.—Puerperal contractions of the uterus, clinically important as a means of control of bleeding and as related to after-pains, have been studied by W. Bickers who has communicated the results to the South Atlantic Association of Obstetricians and Gynecologists. The subjects of study were six primiparae. Each had a normal labour at term and was delivered by low forceps under novocain (procaine hydrochloride) analgesia. The placenta was allowed to separate spontaneously in each case and as soon as the third stage of labour was completed, the vagina was cleaned with tincture of metaphen through a sterile speculum, and a rubber balloon of 100 cubic centimetre capacity was pushed up to the fundus with uterine dressing forceps. The balloon was connected to a mechanical ink-writer recording on a revolving kymograph. The contractions observed were similar in all cases. After the delivery of the placenta they were large, recurring about every three minutes and lasting for about seventy seconds. By the fifth day amplitude, regularity and duration were much diminished and the uterus no longer responded to pituitary extract. By the tenth day the contractions had ceased. Subsequent administration of oestradiol benzoate, by which 1 milligram was given daily for three days, restored the uterine contractions and the sensitivity to pituitary extract.

Complications other than sepsis

Insanity

Progestosterone treatment of puerperal psychosis.—A case of post-partum psychosis treated by progesterone is reported by H. J. Schmidt, who notes the favourable prognosis in this type of insanity and the proneness to recurrence after subsequent labours. In his patient, recurrence of symptoms at the menstrual periods suggested the possibility of endocrine imbalance, on which treatment was based. The patient was a primigravida, aged twenty-one, healthy, well adjusted to married life and wanting a child. Delivery was effected with low forceps and episiotomy after a normal labour of ten hours' duration. The woman left hospital on the fifth day of the puerperium; two days later she showed the first symptoms of a psychosis which became steadily worse. She was readmitted to hospital in which she remained for about five weeks; on discharge she appeared normal. Two weeks after her return home the symptoms recurred; five days later a menstrual period began and after a week the psychosis cleared up. For two weeks she appeared perfectly normal and performed her household duties as usual. Then she relapsed; the menstrual period began on the fifth day, and again after a week the mental symptoms disappeared. The same mental disturbance recurred at the third monthly period but this time cleared up with the onset of the menstrual flow. Each relapse was heralded by slight irritability, otherwise the patient was apparently normal during the phases of sanity. The relation to menstruation seemed to point to hyperaesthism as the factor bringing about relapse. Progesterone therapy was therefore instituted at the time of ovulation, 1 milligram being given daily for three days. Increasing nervousness and irritability were noted and the daily dose was therefore increased to 10 milligrams, this treatment being continued until two days before the expected menstrual period. All mental symptoms disappeared. The author suggests that loss of the progesterone-forming activity of the placenta precipitates post-partum insanity.

Engorgement of the breasts

Early use of methyl testosterone.—S. Duckman and T. R. Turino have treated puerperal engorgement of the breast in fifty cases with methyl testosterone administered by mouth. Other treatment such as restriction of fluids, ice-bags and so on, was not given, because it was essential that any factor which might confuse the results should be eliminated. Testosterone treatment was withheld until the third or fourth post-partum day—that is until the breasts were quite full—because it acts more effectively then. Filling of the breasts indicates that the supply of oestrogen in the circulation is so greatly diminished that it no longer exerts an inhibiting effect upon the pituitary gland. The mode of action of testosterone in stopping lactation is not yet known. Possibly it acts by inhibiting the pituitary gland from liberating prolactin or by antagonizing the latter. The result of testosterone treatment was classified as 'good' when the patient obtained complete subjective and objective relief. A small percentage continued to lactate to a minor degree for several days after the treatment was discontinued but this was not considered a reason for classifying the case as unsuccessful, since the aim of treatment was to put a complete stop not necessarily to lactation but to the pain and discomfort associated with weaning. Results were classified as 'fair' when pain and tenderness were only partially relieved and as 'poor' when no appreciable degree of relief was obtained. Of the fifty patients, forty-four (88 per cent) showed a good result; four (8 per cent) a fair result; and two (4 per cent) a poor result. The total dosage of testosterone employed (the actual substance used was methyl testosterone—the oral brand, oreton M) varied from 60

milligrams to 270 milligrams, but in most cases was 150 milligrams in doses of 30 milligrams every four hours. Subinvolution was noted in 6 per cent of the patients. This incidence is not any higher than that occurring in women who suckle their children.

Puerperal sepsis

History of puerperal sepsis

A century of progress in treatment.—E. F. Daily sketches the changes in theory and practice which have occurred since in 1843 Oliver Wendell Holmes demonstrated the contagious character of puerperal fever. Many of Holmes's contemporaries were not convinced by his reasoning and continued to hold the view, generally prevalent at that time, that puerperal fever is caused by atmospheric conditions, diet or the emotions. At the time when Holmes's essay was published the death rate in the Vienna maternity hospital was 16 per cent. In 1847 Semmelweis, then recently qualified and working in the hospital, stated his belief that the causal element of puerperal fever was conveyed by the doctor's or midwife's fingers, by instruments or sponges or, more rarely, by air. He introduced the practice of washing the hands in chlorinated lime water, and the mortality fell within two years to 1.3 per cent. In 1866 the maternal mortality in French hospitals was about 1 in 29, and in some hospitals was 1 in 7. In 1871 Matthews Duncan found from the statistics of various European hospitals that at least 1 in 120 women died in childbirth. Between one-third and one-half of these deaths were due to puerperal fever. Even at that date, however, Duncan could pour scorn on the idea that the disease might be preventable. It remained for the discoveries of Pasteur and Lister to initiate a tradition of cleanliness in midwifery. In 1905 Cullingworth analysed the British statistics for the fifty-seven years ending 1903 and found that the death rate from puerperal sepsis during that period, far from falling, had actually increased. He drew attention to the deplorable consequences of non-fatal cases. By 1941 the death rate from puerperal sepsis had fallen to 1 in 2,000 in England and Wales, and to 1 in 3,000 in the United States of America. It must be emphasized once more that most of these deaths were preventable.

Treatment of puerperal sepsis

Specific chemotherapy.—N. M. Falkiner points out that chemotherapy has already dramatically altered the maternal mortality rate but that women still die of puerperal sepsis, and in addition deaths occasionally result from agranulocytosis, one of the most serious complications of chemotherapy. In the Rotunda Hospital, Dublin, the method of dealing with puerperal sepsis depends upon the circumstances in which it arises; it may occur as a complication of normal deliveries, or of diseases for which only minor operative interference has been required, or in connexion with difficult labour. In dealing with cases of the first kind the routine is as follows. When the first rise of temperature occurs a cervical swab is taken. Soluseptasine, 10 cubic centimetres of a 10 per cent solution, is given intravenously and then 0.5 gramme doses of prosectasine are given four-hourly. If in twenty-four hours the report on the swab states that a haemolytic streptococcus is present, prosectasine is continued for five days and in some cases additional doses of soluseptasine are given. Another swab is taken before the patient is discharged. If the original culture shows *Staphylococcus aureus*, sulphathiazole is advised. Sulphapyridine is more suitable for infection by *Bacillus coli*, *pneumococcus* or *gonococcus*. Should infection be due to an anaerobic streptococcus, blood transfusion and intra-uterine instillation of glycerin are indicated in addition to the administration of sulphonamides. Patients in these cases do not respond to chemotherapy so well as those who have a haemolytic streptococcal infection and show a special liability to thrombophlebitis and pyometra. In cases of difficult labour, when infection has occurred before delivery, the first step is to determine what organism is responsible. A continuous intravenous drip of 5 per cent glucose solution is started, and every four to six hours 10 cubic centimetres of soluseptasine is added. Immune serum should be given in cases of *Bacillus welchii* infection. Delivery may necessitate lower segment Caesarean section or Caesarean hysterectomy.

EDITORIAL COMMENTARY—Pillars of Treatment in the Puerperium

The puerperium may be regarded as the prolonged post-operative phase of the surgical operation of labour. Such an attitude towards this process has many practical advantages: it stresses the need for antenatal inquiry and treatment (pre-operative investigation), it lays strong emphasis on the importance of careful technique during labour, and it shows the relevance to the puerperal state of all those advances in general medicine and surgery which help to prevent or correct post-operative complications.

With regard to puerperal sepsis, the dazzling achievements of modern chemotherapy have tended to create a sense of false security and to distract attention from the less spectacular methods of prevention which, nevertheless, remain as the most important aspect of the subject. Preventive methods must include (1) proper antenatal care with special emphasis on the fact that the soundness of all organs should be ascertained and on the need to confirm the absence of anaemia; (2) the aseptic and antiseptic conduct of labour with the minimum of manipulation, trauma and blood loss; and (3) the avoidance of exposure to infection during the puerperium by careful nursing and by the strict isolation of all infected patients (J. P. Greenhill, 1942). In addition to these generalizations the following facts may be pointed out. In Philadelphia during the period 1932–42, 308 women died of puerperal sepsis and of these deaths three-quarters were deemed preventable (C. C. Briscoe, 1943). In 50 per cent of cases in which the organism concerned is the haemolytic streptococcus, the source of infection

is the medical attendant, nurse or midwife (Dora Colebrook, quoted by D. Baird, 1942). W. E. Studdiford (1942) has confirmed that an enormous improvement can be expected from the use of sulphanilamide in streptococcal infections, but L. A. Siegel (1942) has shown in a maternal mortality study in Buffalo that sepsis is still the outstanding cause of death in child-bed (25 per cent of all deaths) despite the fact that for three of the five years covered by the investigation chemotherapy and transfusions had been widely used in treatment. It is therefore well to remember that modern chemotherapeutic methods, valuable as they have proved to be, are not capable of eliminating the risk to life when infection has once been introduced into the patient. Without doubt, the vagina is the commonest portal of entry and admits organisms by droplet infection or directly via the fingers or instruments of the attendants—sources of infection which can be eliminated by the use of efficient face masks and by the substitution of rectal for vaginal examination. It has been claimed with some truth that the wider use of rectal examination would save many lives and many hundreds of grammes of sulphanilamide. This method of examination has its limitations, but it will certainly afford reliable information concerning the progress of labour as measured by the level of the presenting part and the rate of its descent through the birth canal.

With regard to the prevention of infection, H. Speert (1943) has recently demonstrated again that sulphathiazole, and sulphadiazine, like sulphanilamide, diffuse readily across the placenta and appear almost immediately in the foetal blood in which they remain in effective concentration for six hours or more. The drugs also appear, although more slowly, in the liquor amnii, and therefore caution must be observed in regard to dosage, for A. M. Ginzler and C. Chesner (1942) have reported a case of fatal toxæmia in an infant as a result of transmission of sulphanilamide during labour. L. P. Rojas (1942) advocates the prophylactic use of sulphanilamide preparations in labours of more than twenty-four hours' duration, in cases of premature rupture of the membranes, and also in cases in which many vaginal examinations have been made. The drug is given before delivery in doses of 5 to 6 grammes a day. Such prophylaxis may prove to be of great value and it is well worth a trial in domiciliary cases of the suspect type. H. E. Anderson, H. L. Gardner, M. F. Gunderson and J. M. Slack (1942) have drawn attention to the prophylactic value of impregnating the packs with sulphanilamide when tamponade is used to control hæmorrhage. They found that although the drug was absorbed to only a limited extent into the blood stream, its local action had a pronounced effect upon the flora of the genital tract and actually inhibited the growth of hæmolytic streptococci.

After a massive hæmorrhage, heparinized plasma has been found to be the safest and most effective blood substitute; the replacement of erythrocytes is unnecessary according to the results of animal experiments carried out by A. C. Ivy and his associates (1943). These workers also found that when citrated plasma was given in large amounts the quantity of citrate frequently gave rise to toxic effects. When used clinically, citrated plasma must not be given in unlimited quantities, it should be given slowly and the label on the container should draw attention to the toxicity of the sodium citrate content. Certain women in the puerperium display a particular sensitivity to the so-called Rh factor and great care must be exercised in the choice of the donor when such patients require transfusion. In all cases the effects of previous transfusion, if any, must be ascertained and any unusual reaction duly noted. Very special attention must be paid to patients who give a history of repeated abortions and to those who have borne children affected with erythroblastosis. The only safe method for patients with these histories is to give them blood from donors in whom the Rh factor is known to be negative; indeed it would be better to use such special donors for all puerperal cases. Apart from the replacement of blood lost, repeated transfusions in small amounts are often of the greatest therapeutic value in puerperal infection, especially when used in conjunction with sulphanilamide treatment.

Papars continue to appear dealing with the effect of sex hormones upon breast engorgement and the inhibition of lactation. J. I. Kushner (1942) has shown that when required, lactation can be inhibited by the oral use of methyl testosterone, three 10-milligram tablets thrice daily for three days being a sufficient dosage. The use of stilboestrol given by the mouth is still popular for its similar effect and when combined with local pressure and ice-packs it seems to be an ideal way of suppressing lactation (E. M. Jeppson, H. Y. Kasabach and A. E. Kanter, 1942). Five milligrams daily, or even more, may be given, and it is interesting to note that women in the puerperium are less sensitive to the side-effects of stilboestrol than are non-puerperal women.

For after-pains, progesterone has proved to be valuable, but, as E. C. Hamblen (1943) has pointed out, other and cheaper methods such as ergot therapy are just as effective. Again, as Bickers has shown, uterine contractions no longer occur after the tenth day and this coincides with the fall in the oestrogenic blood level. Administration of oestrogens will restore mobility and once again sensitize the uterine to pituitary extract. Therefore for the treatment of puerperal hæmorrhage after the fifth day these substances should be used in combination.

—A. LEYLAND ROBINSON.

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RADIOLOGY IN DIAGNOSIS AND TREATMENT

See also B.L.M.P., Vol. X, p. 456; and Cumulative Supplement, Key Nos. 1340-1343.

Methods of radiography

Fluorescent screen

Localization of foreign bodies—V. V. Bourke describes a new method of localization of foreign bodies by X-ray examination, based on the principle of parallax. Three pieces of apparatus are required. (1) A fluoroscopic screen which can be moved horizontally in the long axis of the table and at a right angle to it. It is ruled with one longitudinal line through its centre and a number of parallel lines crossing the centre line at right angles. The X-ray tube moves with the screen so that the vertical ray is always centred on the centre point of the screen. (2) An arrangement of calipers, the arms of which are tipped with lead and which can be opened or shut, raised or lowered. The combined apparatus is mounted in such a way that when the tube box is moved the screen and the calipers follow it, except when the tube box is released for the parallax procedure. Superimposed on the screen are sliding markers which can be moved to right or to left of the shadow of the foreign body. (3) For interpreting the X-ray appearances a steel rod formed into a semicircle is provided with two sliding pointers at the tips of the semicircle and a third pointer which can be moved anywhere on the arc. The pointers are marked in inches. When the investigation is carried out the screen and caliper combination is placed over the part to be examined and the screen is moved until the shadow of the foreign body falls on the centre point of the screen. The arms of the calipers are moved until the tips touch the skin surface on either side; the screen is then fixed. The tube is released and shifted backwards and forwards and the calipers are raised or lowered until the tips are in the same plane as the foreign body. At the points where the tips touch the skin indelible marks are made. The readings on the calipers are taken, each half will register the distance from the foreign body to the skin surface on that side. A straight line between the tips will pass through the foreign body. The surgeon sets the two pointers marking the diameter of apparatus no. 3 for the readings given by the calipers and places the tips in contact with the marks on the skin. The third pointer is then lowered to the point at which it is desirable to incise the skin, it will always point to the foreign body.

Contrast radiography

Fatal diodrast (diodone) administration—Twenty-six deaths occurring after intravenous administration of contrast media for radiographical examination, and not already recorded in the literature, are reported by L. P. Pendergrass, G. W. Chamberlin, E. W. Godfrey and E. D. Burdick. The data were collected by means of a questionnaire sent to 1,048 workers (radiologists and urologists). The total number of examinations was 661,800, so that the fatalities represent a percentage mortality of 0.0039. The deaths fall into two groups, one (ten patients) in which death occurred immediately from idiosyncrasy to the drug or from colloidal shock, and one in which death was delayed and presumably was due to pre-existing renal damage. All immediate deaths occurred after the administration of diodrast (diodone). None of the patients had been tested for diodrast sensitivity. One patient had a personal and family history suggestive of allergy, one was a child, aged 20 months, who received 15 cubic centimetres of 35 per cent diodrast. Non-fatal reactions were reported in a number of cases. The delayed deaths occurred after the administration of various preparations, and direct connexion with the examination could not be proved. The authors suggest that contrast media should not be given to patients with significant impairment of renal function, and they should be used cautiously in patients with a history of allergy. Epinephrine (adrenaline) should be available for instant use. Not more than 50 cubic centimetres of 70 per cent diodrast should be given on one day. The use of pitressin (pressor principle of posterior pituitary extract) to dispel intestinal gas appears to increase the likelihood of subsequent reactions, and is best avoided.

Roentgen-cinematography of the cardiac circulation.—By using thorotrast as a contrast medium, N. Westermarck has obtained roentgen-cinematographic records of the circulation

through the heart and great vessels of the rabbit. Concurrent electrocardiography permitted the X-ray appearances to be compared with the electrocardiographic findings. Thorotrast is deposited very slowly from the blood, thus the injection can be made sufficiently gradual to avoid influencing the venous return to the right auricle, and film records can be made for about an hour afterwards. Screening is begun before the injection is started, and the course of the thorotrast is watched. By this means the average circulatory period through the pulmonary circulation was estimated as being 1.7 seconds; it was longer in animals with slower pulse rates. The flow is more rapid in the aorta than in the pulmonary artery, since the rate is related to the comparative diameters of their respective ostia. Comparison with the electrocardiogram showed that the auriculo-ventricular valves are open only during the PQ interval, that is that blood enters the ventricle during presystole only. Blood flows into the auricle throughout the cardiac cycle, but more rapidly at the beginning of diastole. The semilunar valves open at the beginning and close at the end of T. Ventricular contraction is a progressive movement, involving successively the interventricular septum, the apex and the conus arteriosus; contraction begins at the Q wave and relaxation at the P wave.

Systematic radio-diagnosis

Alimentary tract

Recent observations ---M. Feldman has reviewed the literature for 1941 dealing with the radiology of the digestive tract (1) *Oesophagus*. Of congenital atresia and fistula many cases are reported. In one case a tracheo-oesophageal fistula was demonstrated by the injection of lipiodol into the trachea. Oesophago-pleural fistulae may be acquired, as a result of empyema. Herniation of the stomach through the oesophageal hiatus, and thoracic stomach have been observed with increasing frequency, the latter condition is associated with an abnormally short oesophagus. In 48.4 per cent of one series of cases of thoracic stomach diverticulosis of the colon was also present. Benign tumours of the oesophagus, which were mostly of the pedunculated type, have been reported. Oesophageal obstruction due to gummatous disease has also been observed. (2) *Stomach*. Feldman's new sign of pyloric obstruction consists in the appearance of the entire stomach outline as a soft tissue shadow, due to the retention of fluid in large quantities. The increasing use of gastroscopy in gastritis and the comparison of the findings with those of radiology have shown that the latter are often negative or are erroneous. The number of recorded cases of peptic ulcer in children has steadily increased, probably because children are examined radiologically more often now than formerly. Diverticula of the stomach are being recognized with greater frequency. In distinguishing between organic stenosis and spasm of the pylorus, the relative quantity of barium which remains in the stomach after four hours is shown to be a valuable guide. In one series, of the organic cases, 92.3 per cent showed retention of 60 to 100 per cent whereas of the cases of pylorospasm, 91.3 per cent showed retention of only 25 per cent or less. Connective tissue tumours of the stomach, especially leiomyomas, have been recorded with increasing frequency. (3) *Duodenum*. Work has been done upon the radiographical appearances of the normal duodenum. Several cases of giant ulceration have been reported; the appearances may be misleading, in that the ulcer crater may be taken for the normal bulb and, of ten such cases which were reported, six were in fact misinterpreted. (4) *Intestines*. The normal and pathological appearances of the terminal ileum have been studied by a number of workers. Regional ileitis can be diagnosed by means of X-rays in the majority of cases (eleven out of thirteen were diagnosed in one series). Diverticulitis of the jejunum has been reported. Tumours of the small intestine have been observed. Congenital obstruction of the small intestine is not uncommon, and the plain film can be of value in diagnosis, as it is also in intussusception. The use of drugs to eliminate gas in the colon has been the subject of investigation. Anomalies of the appendix, for example double appendix, are reported. Abnormalities of motility of the gastro-intestinal tract have been observed in cases of vitamin B deficiency and of hyperthyroidism. (5) *Biliary tract*. Cholecystography has increased the frequency with which diverticula and tumours of the gall-bladder have been recognized. Cholangiography has received considerable attention; it may reveal stenosis, stones or diverticula of the ducts. Internal biliary fistulae have been recognized radiologically by the presence of air in the biliary tract. (6) *Pancreas*. Indirect evidence of enlargement of the head of the pancreas from any cause is furnished by deformation of the duodenal shadow. Direct evidence of pancreatic lesions is less seldom obtained, but calcified tumours are occasionally visualized. (7) *Liver*. Enlargement is seen in cases of hydatid cyst and occasionally visible calcification occurs in the cyst wall.

Respiratory tract

Mass miniature radiography in Australian children ---The civic authorities of Adelaide have planned to undertake a survey by mass miniature radiography of 30,000 school children. The scheme has met with much adverse criticism on grounds that are stated in a paper read to the local branch of the British Medical Association by D. R. W. Cowan. They are as follows. (1) In many cases of early pulmonary tuberculosis the focus of disease is too small or too soft for demonstration by clinical or radiological examination. He cites the results of routine examination of nurses, which has been practised since 1940 at the Royal Adelaide Hospital. Nurses are examined on entry and at intervals throughout their employment in the hospital. An X-ray examination is made every year, and in the case of Mantoux negative reactors every three months. It is found that in a large proportion of persons who change from Mantoux negative to Mantoux positive while thus under observation, no difference can

be detected between the skiagrams taken before and those taken after infection occurs. (2) That tuberculosis in Australian school children is not sufficiently common to justify the undertaking of mass radiography. A series of 1,363 apparently healthy young adults is cited, in which only six cases of active pulmonary tuberculosis were discovered, not one being of the 'open' type. (3) Too much value may be attached to radiological examination as compared with the value of clinical findings. A case is quoted of a man who was accepted for the Army after full examination, including radiography, although, as he failed to disclose to the examining board, he had been attending a chest clinic and had had four attacks of pleurisy in the preceding two years. The paramount importance in children of clinical examination, with tuberculin testing, is urged. Mass radiography is best reserved, in the author's opinion, for the detection of active pulmonary tuberculosis in adults, with the object of disclosing the presence of the open infectious lesion.

Miniature radiography.—P. Kerley claims that if two views of the chest, namely antero-posterior and postero-anterior, are taken, the degree of diagnostic accuracy which can be attained with full size films is also attainable by miniature radiography. The taking of two views increases wear and tear of the apparatus and diminishes the number of patients who can be dealt with per hour, but such disadvantages are of minor import. When the standard postero-anterior position only is used, lesions situated toward the back of the lungs are shown badly, if at all, on the 35-millimetre film, owing to the short distance (30 inches) at which the radiograph is taken. By using both positions, moreover, the risk of an early tuberculous focus being hidden by a rib shadow is greatly reduced.

Renal tract

Excretion urography.—Lecturing to the Radiological Society of North America E. P. Pendergrass took as his subject the value of excretion urography as a test of urinary function. Of the radio-opaque substances used, diodrast (diodone), hippuran (sodium ortho-iodo-hippurate) and neo-iopax (iodoxylum) reach the urine by filtration through the glomeruli and also by excretion through the tubules, skiodan by glomerular filtration only. If clinical tests of kidney function have yielded normal results the diodrast or skiodan clearance is very satisfactory. If, however, clinical evidence has been obtained of kidney disease a contrast medium which is eliminated largely by the tubules is preferable. The normal clearance time, as shown by a dense shadow of the kidney pelves and bladder, does not exceed forty-five minutes. Often the dye is to be seen five minutes after it has been injected. It is questionable whether urography is safe when the urea clearance is below 30 per cent. Urography also enables the normal peristaltic movements of the renal pelvis to be viewed and recorded cinematographically. The emptying time of the renal pelvis varies considerably even in normal subjects. Studies after urination demonstrate the degree of completeness with which the bladder has been emptied. In the absence of obstruction the bladder shadow practically disappears.

Nervous system

Encephalography in head injuries.—H. Davies briefly describes a series of cases of head injury which were investigated by encephalography. In all but fourteen the air was introduced by the cisternal route; when the lumbar route is used more air must be injected. The air was filtered by being drawn into the syringe through sterile cotton-wool. No serious symptoms followed in any case. Headache, pallor and sweating occurred during the injection in the majority of patients, and nausea in from 50 to 60 per cent, with vomiting in about 25 per cent; about six patients who had already had epileptic fits had one during the injection. Radiological abnormalities are not seen in cerebral concussion. Cerebral contusion is associated with atrophy of the affected portion of the brain, which is probably due to the circulatory disturbances produced by damage to small blood vessels; this leads in its turn to ventricular dilatation with or without expansion of the cortical channels. Injury to and occlusion of larger vessels may account for the condition known as traumatic porencephaly, in which cysts are formed in the brain substance and are visible in the X-ray.

Examination of skull

The pituitary fossa.—H. Burrows, A. J. L. Cave and Kathleen Parbury record the results of radiological examination of the skulls of four groups, white males, white females, negroes and negroes, in order to assess the dimensions of the pituitary fossa. Of the 100 skulls selected for this investigation fifty were of African negroes of known locality and fifty were British from an old (post-mediaeval) London burial ground. Silhouettes of the pituitary fossa from the four groups are reproduced and deductions are drawn with caution. In the material examined the estimated area of the pituitary fossa in males exceeds that in females in both the British and the African crania. Another point of interest is the wide individual variation in size and shape of the pituitary fossa. Very probably this variation depends, to no small degree, upon purely anthropological or racial factors (type and build of cranium) as well as upon sexual and intrinsic (vascular and other) factors and the matter is worthy of further attention. Further research was intended but has been delayed by the lamentable damage done to the Museum at the Royal College of Surgeons.

Endocrine organs

Differential diagnosis by radiography.—P. J. Connor and F. J. Maier draw attention to the potentialities of radiography in the diagnosis of various endocrine diseases. Some examples are referred to below. In acromegaly the diagnosis is confirmed by X-ray examination of the sella turcica and even in the earlier stages changes such as increase in size of the frontal and

occipital protuberances, broadening of the phalanges and so forth may be detected by X-ray examination. Radiography may serve to differentiate primary from secondary gigantism, and also to distinguish between endocrine (thyroid or pituitary) dwarfism and non-endocrine dwarfism resulting from achondroplasia, rickets, renal rickets or scurvy. In all these conditions characteristic appearances may be seen in the X-ray plates, for example epiphyseal changes in rickets, elevation of the periosteum and Frankel's lines in scurvy. In thyroid gland disorders radiographs are of little value, except to show a retrosternal extension. In Addison's disease radiography may show calcification of the adrenal glands. In hyperadrenalism retrograde pyelography may show distortion or malposition of the kidney, and injection of air into the perirenal space may demonstrate an enlargement or tumour of the adrenal gland. Enlargement of the thymus gland can be demonstrated only by X-ray examination

Radiotherapy

X-ray therapy

Estimation of dosage —F. T. Farmer describes the two methods of measuring X-ray dosage which are in use at the Middlesex Hospital and a modification of these which has been tried experimentally with encouraging results. All the methods depend on the ionization of air by X-rays, and indicate dosage in roentgens. (1) The Mekapion or Hammer type of dosimeter has been found to be capable of great constancy of performance, often not needing any adjustment after weeks of use, and lasting for a long time; the high initial cost thus appears to be justified in circumstances in which regular estimations are required. It possesses, however, three disadvantages (a) a source of error amounting to from 5 to 10 per cent is introduced by the small space between the centre of the chamber and the patient's skin, the amount of error varying with the focal distance; (b) the instrument exerts some screening effect, so that a portion of the treated area receives less than the proper dose; and (c) it cannot be used when the area to be treated is very small. (2) Tube output calibrations; the dose given is calculated from the duration of the treatment and the known output of the tube. The method depends upon the constancy of the latter factor, which with certain tubes may fluctuate seriously. It does not give as accurate a measurement as the dosimeter gives when the treated surface is curved or irregular, although accuracy may be increased by packing round such areas with bolus. But it eliminates errors due to separation of the dosimeter from the patient's skin, and it can be used for small areas. (3) A modification which has been tried is the fixed chamber integrating dosimeter, in which the ionization chamber is fitted in the output aperture of the X-ray tube. It is capable of giving accurate measurements for all applicators and focal distances, and it eliminates the risk of damage to the thimble chamber through continued handling. It possesses the same drawbacks as the calibration method in regard to curved surfaces, and it does not take into account mistakes in the choice of applicator.

Irradiation of the entire body —Irradiation of the entire body was first employed in the hope of destroying early cancerous metastases, since then it has been used for a number of other conditions. F. G. Medinger and L. F. Craver review a series of 270 cases treated in this way at the Memorial Hospital, New York, during the ten-year period ending 1940. The method used was that of A. C. Heublein, involving prolonged continuous irradiation with hard rays of low intensity at long target-skin distance. The unit has been placed in the wall between two single-bed rooms so that two patients can be treated simultaneously. The following factors are employed: 185 kilovolts, 1 milliamperes, 5.5 millimetres copper equivalent; the distance from the X-ray tube to the patient is 3 metres. The output is 0.86 roentgen per hour. The hours of treatment are registered by a recording meter outside the rooms, and total twenty or twenty-one in each twenty-four hours. In all cases treated the diagnosis had been established beyond doubt. They included the following (1) Hodgkin's disease, ninety-four cases, treated by localized X-ray therapy plus total irradiation. Total irradiation alone is usually insufficient to produce complete remission of the disease. The five-year survival rate in this series was 32 per cent, as compared with 12 per cent in untreated Hodgkin's disease. This improved survival rate is particularly encouraging because the cases as a group were advanced. (2) Lymphosarcoma, thirty cases. Local and general irradiation was given. The average time of survival was 24.2 months, while for lymphosarcoma treated by all methods it is 11.8 months. (3) Lymphatic leukaemia, seventy-six patients. Irradiation did not materially prolong life but in chronic cases the period of useful life was increased. (4) Myelogenous leukaemia, twelve cases. Total irradiation possesses no advantages over local irradiation in prolonging life, but prolongs the period of useful life. (5) Polycythaemia vera, five cases, two with associated myeloid leukaemia. Either total or local irradiation appears to control the disease for long periods. (6) Mycosis fungoides, six cases. Brief and incomplete palliation was obtained. (7) Multiple myeloma, eleven cases. The survival time appeared to be increased. (8) General carcinomatous or sarcomatous metastases, thirty-five patients. The results were discouraging. The authors conclude that total irradiation is a useful adjunct to local irradiation in the lymphomatoid diseases. Complications, including purpura, haemorrhage and leucopenia, may preclude continuation of treatment. Leucopenia is the most serious, and a careful watch must always be kept on the blood.

Radium therapy

Carcinoma of the vagina. —M. Lederman and W. V. Mayneord discuss the difficulties associated with radium treatment for cancer of the vagina. The development of a reliable technique is hindered by the comparative rarity of the disease, by the advanced stage in which it is

usually seen, and by the proximity of the bladder and rectum. Only seven primary cases have been treated at the Royal Cancer Hospital during the eleven years ending 1940; two patients have survived for three years and one has survived for more than five years. Treatment for choice should include both the local application of radium and telerradium or high voltage X-ray irradiation to the lymph gland areas of the groins and pelvis. For lesions of the upper third of the vagina the methods of local application are the same as those for cancer of the cervix; for the lower two-thirds special applicators are constructed. If the vagina is not too much narrowed, that is if it has a diameter of at least 2 centimetres, a stent mould is taken, with the patient under anaesthesia in the lithotomy position. The lower end of the mould is shaped to fit over the vestibule and a hole is punched opposite the urethral orifice. The treatment area is marked on the stent mould with a skin pencil. A plaster cast is made from the mould and is divided longitudinally; sheet lead, 2 centimetres thick, is then cut and shaped to each half. The treatment areas are marked on the lead with a sharp point. The radium foci are fixed to the inner surface of the applicator with wax and the two halves of the applicator are soldered together. Further screening is afforded by coverings of oiled silk and rubber. The best way of holding the applicator in position is by means of a metal tube inside a rubber catheter, passed through the hole in the applicator into the bladder. The labia minora are packed or stitched out of the way. Two or three treatments are given at intervals of from two to three weeks. The total dosage depends upon the extent of the disease and the tolerance of the tissues. When the lumen of the vagina is much narrowed the radium is applied by means of a bougie containing tubes in tandem. If the bladder or urethra is involved further radium is placed in the urethra or is implanted in the base of the bladder after suprapubic cystotomy. If the rectum is involved palliative external irradiation is preferable to intracavitary applications.

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RECTUM DISEASES

See also B.E.M.P., Vol. X, p. 502, and Cumulative Supplement, Key Nos. 1346–1356.

Rectal incontinence

Treatment

Surgical repair of the sphincter ani—P. C. Blaisdell describes a multiple-stage plastic operation which was devised by him for the repair of large defects of the sphincter ani. The cases for which the operation is recommended are those in which up to about half the muscle has been destroyed, so that the two widely separated ends could only be brought together under excessive tension. The amount of muscle loss can be estimated sufficiently accurately by noting the extent of skin which is smooth and not thrown into folds. The procedure is as follows. A J-shaped incision is made on each side enclosing each end of the divided muscle, with a straight limb extending inwards and backwards (or forwards) from the middle of the hook of the J toward the middle line. No attempt is made to find the ends of the muscle, but flaps are cut which are sufficiently deep to ensure that the ends are included. The two muscle-bearing flaps are advanced and are sutured into the gap left by opening up the straight limb of the incision. When healing is complete the procedure can be repeated, if necessary, several times, depending upon the extent of the defect, and at each stage the muscle ends are brought closer to one another until they are in apposition. Buried sutures of fine wire are used and sulphonamide powder is left in the wound. Results are not given in detail but are said to be extremely successful.

Carcinoma

Other rectal lesions

Carcinoid tumours: Ersparmer's pre-enterochrome cells.—A. P. Stout records six cases of carcinoid tumours of the rectum, five of which differed microscopically from the ordinary carcinoid tumours of the vermiform appendix and the small intestine. Their altered histological picture is due to the presence of the cells described by V. Ersparmer as pre-enterochrome cells, derived from the cells of the tubular mucous glands. Stout collected the following car-

cinoid tumours of the large intestine: caecum—4 carcinoids, all multiple; colon—10 carcinoids, one multiple; rectum—12 carcinoids, two multiple.

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REHABILITATION

In industry

Methods of restoring working capacity

In a Hunterian lecture H. F. Griffiths discusses the treatment of the injured manual worker. The aspiration of treatment in any injured person is to obliterate all physical and mental effects of the injury, but this is an unattainable standard and the author suggests that restoration of working capacity should be made the criterion of recovery. Treatment aims at restoring the power of movement which the workman has lost as the result of the injury, and progress is estimated by the improvement in strength of contraction of the muscles concerned. The first essential is a degree of anatomical reconstruction of the injured part such as will enable the muscle to act to the best mechanical advantage. This does not necessarily imply exact reproduction of the *status quo ante*. For example, after a compound fracture associated with muscle damage some shortening of the bone may offer the best conditions for securing maximum muscular power. Muscle action also demands an adequate circulation and this in its turn depends not only upon the arterial supply but also upon the venous return. Unless the venous flow is unimpeded stagnation occurs in the capillary system with oedema and matting together, by deposited fibrin, of the tendons and muscles. Deficient venous return is the most important factor in the production of stiff joints after an injury. A vicious circle may be set up here, because venous return depends almost entirely on the pumping action of contracting muscles and muscular action upon a proper venous return. The purpose of all treatment is to secure normal muscle action. The development of muscular power may be likened to a ladder. On the lowestmost rungs power is produced by direct stimulation of muscle cells. The next step is typified by the nerve-muscle preparation, in which contraction results from indirect stimulation. On the next rung are situated simple spinal reflexes, above that come the more complex unconditioned reflexes and on a higher rung again the conditioned reflexes. The final step brings us to deliberate action. Power-reducing factors may operate at any level, and the aim of treatment is to eliminate these factors and lead the man back up the ladder of power from the point to which his injury has precipitated him. Only exercise can restore power, and it must be continuous throughout a working day. Training should be based on simple reflex action at first, later upon conditioned reflexes, finally upon deliberate movements.

Griffiths, H. F. (1943) *Lancet*, **1**, 729.

RHEUMATIC INFECTION. ACUTE

See also B.E.M.P., Vol. X, p. 639; and Cumulative Supplement, Key No 1380.

Aetiology

Class incidence

Statistical survey on juvenile rheumatism—Social conditions play a recognized part in the aetiology of juvenile rheumatism, and in order to assess the aetiological significance of them, J. N. Morris and R. M. Titmuss, members of the Committee for the Study of Social Medicine, have examined statistics relating to acute rheumatism and rheumatic heart disease. The mortality from acute rheumatism has been falling for many years, although the figures are less satisfactory for children under fifteen than for other age groups. The mortality from rheumatic heart disease is difficult to estimate accurately because the classification used in compiling vital statistics is based almost entirely upon morbid anatomy, not upon aetiology. From their examination of the clinical evidence available, the authors conclude that rheumatism now causes about 10 per cent of all deaths from heart disease, and nearly 100 per cent of those from heart disease occurring in persons under forty, juvenile rheumatism in general is responsible for about 2 per cent of all deaths in England and Wales, and for 10 per cent of deaths occurring between five and forty-five years. As regards incidence, the authors estimate that there are nearly 200,000 cases of rheumatic heart disease in Great Britain, and therefore juvenile rheumatism probably comes first among infections as a cause of chronic illness and disablement. The prevalence rises with the degree of poverty, in present circumstances it can best be estimated from a study of the mortality from rheumatic heart disease. Between the ages of twenty and thirty-five the mortality rises steeply with decline in social status; at higher ages the difference is less conspicuous. The poorer districts of the country show a higher mortality than do the more prosperous areas. Mortality on the whole increases with density of population and seems to be the result of the greater poverty in large towns; it is as high in depressed rural districts as in the worst urban areas. Damp appears to be unimportant when living conditions are otherwise satisfactory. The authors' conclusions support the view that the factors responsible for juvenile rheumatism are those associated with low standards of housing, of clothing and of feeding. There is not any clear evidence that overcrowding increases mortality, and, as is pointed out in a leading article commenting on the authors'

conclusions, this might indicate that acute rheumatism does not spread by droplet infection, and that poverty plays its part only after infection has been acquired. The disease must clearly be regarded as being preventable, at least to a large extent.

Bacteriology and morbid anatomy

Aetiological factors

Juvenile rheumatism.—R. Miller in his Lumleian lectures discusses the problems of juvenile rheumatism. The disease is agreed to be a general infection, although agreement has not been reached concerning the organism responsible. A streptococcus morphologically indistinguishable from streptococci normally inhabiting the alimentary tract has been found repeatedly in cases of rheumatism, but it is difficult to explain the peculiar histology of rheumatic lesions on the basis of a streptococcal infection, and it has been suggested that some additional factor, for example a virus or an allergic tendency, may be at work. Acute rheumatism is often preceded by tonsillitis. The usual history is that for several months the child has had recurring mild attacks of sore throat with rheumatic pains, then an acute attack of tonsillitis and finally, in from three to twenty-one days later, a fully developed attack of acute rheumatism. In tonsillectomized children early attacks of rheumatism tend to be less severe, and to be limited to chorea without carditis; the incidence of this complication depends not only upon the number of attacks but also upon the virulence of the disease. Valvular infection is probably brought about through the coronary circulation. Chorea may occur without evidence of rheumatism but, in the author's opinion, this should always be regarded as a rheumatic manifestation. Chorea which is apparently non-rheumatic may be the only sign of a modified rheumatic infection. Choreic symptoms are seen in nearly all cases of acute rheumatism. Subcutaneous nodes signify a severe infection. Pneumonia may arise from compression of the lung by the enlarged heart, and pleurisy as an extension of rheumatic pericarditis. Rashes are not a pathognomonic sign of rheumatism but may accompany it. Juvenile rheumatism goes hand in hand with poverty; removal of children from poor homes to residential schools almost abolishes the disease. Some evidence exists that a damp house is a predisposing factor. Tonsillectomy has been found to reduce significantly the incidence of acquired heart disease, and is advisable in all cases of acute rheumatism when the state of the heart permits. Salicylates are effective in the acute, useless in later stages, sulphonamides are ineffective. Subsequent treatment is best carried on in special supervisory centres. Residential treatment in homes or hospital schools is needed for the most severe cases.

Diagnosis

In children

Classification of symptoms and signs.—The diagnosis of acute rheumatism in children appears to present many difficulties, judging by a series of cases analysed by A. E. Hansen. In one-third of the cases the initial diagnosis was wrong. The symptom which most often caused confusion was abdominal pain. In twelve instances the predominance of this pain led to a diagnosis of appendicitis and in seven others to the rheumatic fever being overlooked. In some cases the appendix was removed, but as the author points out, genuine appendicitis may co-exist with rheumatic fever and if serious doubt is felt exploration is amply justified. The major symptom was pain in the extremities in thirteen patients sent to hospital, their condition being diagnosed as poliomyelitis, acute osteomyelitis, tuberculosis and various other diseases. Three children with urinary symptoms were labelled 'acute nephritis', one 'pyelitis'. Skin rashes led to erroneous diagnosis in three. Other children were sent in with a variety of diagnoses including septicaemia, infective endocarditis, pneumonia, undulant fever, psychosis. To avoid delay and inadequate treatment it is essential to realize that rheumatic fever does not always conform to the classical type. In an outbreak of rheumatic fever in a children's home, reported by S. P. Dikowsky, E. Stevenson and J. M. Campbell, the cases (eighty-eight out of a total population of 561 children) were divided into three groups as follows. (1) Patients with severe polyarthritis, fever and high sedimentation rate, sometimes accompanied by rheumatic erythema, nodules and carditis. (2) Those with moderate or subacute polyarthritis, sometimes accompanied by rheumatic erythema, nodules and carditis. (3) Younger children with cardiac manifestations, fever, quick pulse, high sedimentation rate, pallor, epistaxis, aching legs and abdominal pain. In twenty-one cases the attack came on after a haemolytic streptococcal infection of the throat, of which an epidemic occurred in the home six weeks before the outbreak of acute rheumatism. Familial disposition appeared to be an important factor in susceptibility.

Occurrence in children

Main factors in the diagnosis.—C. B. Perry points out that while acute rheumatism in children is seldom mistaken for anything else except when the onset resembles acute appendicitis, the following rarer diseases are frequently mistaken for acute rheumatism: infantile syphilitic epiphysitis or scurvy; Still's disease; acute poliomyelitis; Henoch-Schönlein purpura; acute leukaemia; acute osteomyelitis; brucellosis; meningococcal septicaemia. Typical rheumatic arthritis 'flits' from joint to joint and the pain is strictly localized to a joint. Pain and fever quickly subside under adequate doses of salicylate of sodium. A history of recent upper respiratory infection is common. Cardiac involvement occurs in nearly 75 per cent of children.

Treatment**Remedial**

Chemotherapy in the prevention of recurrences in children.—A four-year study of sixty-four rheumatic children has been carried out by A. E. Hansen, R. V. Platou and P. F. Dwan to determine the value of sulphonamides in averting recurrences. Sulphanilamide was given daily from October to June for one or two seasons in a total of seventy-eight 'season-cases'. Sulphathiazole or sulphadiazine was substituted in a small minority of cases during the third and fourth seasons. Only two rheumatic recurrences were observed in the seventy-eight treated patients, whereas twenty-one recurrences occurred in an untreated control group of forty-six season-cases. Most of the patients treated by sulphonamides improved in general health. The cardiac involvement was estimated not to have increased in any; it remained stationary in fourteen and decreased in six. Among the controls the cardiac involvement increased in three, remained stationary in twenty-one and decreased in one. Toxic manifestations were rare and no electrocardiographic evidence was obtained that sulphonamides damage the myocardium.

Ditkowsky, S. P., Stevenson, E., and Campbell, J. M. (1943) *J. Amer. med. Ass.*, **121**, 991.

Hansen, A. E. (1943) *J. Amer. med. Ass.*, **121**, 987.

— Platou, R. V., and Dwan, P. F. (1942) *Amer. J. Dis. Child.*, **64**, 963.

Miller, R. (1942) *Lancet*, **2**, 563.

Morris, J. N., and Titmuss, R. M. (1942) *Lancet*, **2**, 59.

Perry, C. B. (1943) *Practitioner*, **150**, 213.

RICKETS

See also B.E.M.P., Vol. X, p. 661

Rickets**Pathogenesis and morbid anatomy**

Relation of acidosis and late rickets.—J. D. Boyd and Genevieve Stearns discuss the relation of acidosis to late rickets, and conclude that the sequence of events is chronic renal dysfunction, excessive loss of fixed bases, depletion of calcium reserves and rachitic changes in the bones. They cite the case of a girl, aged eleven and a half years, who suffered from weakness and difficulty in walking. There was varus deformity of one knee and valgus of the other, enlarged epiphyses, and X-ray evidence of active rickets. The girl was of average height and weight for her age. The daily output of urine was about double the normal amount, the specific gravity being low and varying only by four points during a twenty-four hours' period; the urine reaction was neutral, and subsequent studies showed that the child was unable to secrete an acid urine. The chloride content and alkali reserve of the blood were about half the normal. The child was given daily a quart of milk, three teaspoonfuls of cod-liver oil and one and a half teaspoonfuls, subsequently increased to three teaspoonfuls, of sodium bicarbonate. The rachitic lesions healed satisfactorily but the polyuria with low specific gravity and neutral reaction persisted. During the three years in which the patient remained under observation she had, at intervals, attacks of muscular weakness and paraesthesia, the nature of which could never be explained, and in one of these attacks she died. Histological evidence of damage to the renal tubules was not obtained *post mortem*, and it is concluded that the disturbance of renal function had its origin in some lesion of the regulatory organs, possibly of the di-n-cephalon.

Boyd, J. D., and Stearns, Genevieve (1942) *Amer. J. Dis. Child.*, **64**, 594.

SALIVARY GLAND DISEASES**Tumours****Morbid anatomy**

Histological classification.—The histological variability of the so-called mixed tumours of the salivary glands is explained, according to W. H. Sheldon, by proliferation of one or both of two kinds of cell—the secretory epithelium and the myo-epithelium; by degeneration or pathological activity of the tumour cells, which gives a myxomatous appearance to the stroma; and by metaplasia of connective tissue into cartilage or bone. The myo-epithelium consists of peculiar contractile cells (basket cells) lying between the acini of the gland. The tumours fall into four groups: (1) non-cancerous growths of the glandular epithelial cells; (2) growths, mostly non-cancerous, derived from both epithelium and myo-epithelium; (3) basket cell growths, non-cancerous or of low malignancy; (4) malignant epithelial cell growths.

Sheldon, W. H. (1943) *Arch. Path.*, **35**, 1.

SCIATICA

See also B.E.M.P., Vol. XI, p. 26; and Cumulative Supplement, Key No. 1389.

Diagnosis and differential diagnosis**X-ray investigation**

Analysis of radiographs in low back and sciatic pain.—In studies of low back and sciatic pain X-ray examination frequently reveals abnormal conditions the clinical importance of which

may be difficult to assess. In an endeavour to estimate their significance, E. A. Brav, S. Bruck and J. M. Fruchter have compared the radiographical findings in a series of seventy cases of low back pain with those in thirty-five people with painless backs. The first group included fifty-two females and eighteen males of ages varying from seventeen to seventy-three years. The second group consisted of twenty-nine females and six males of ages ranging from fifteen to sixty-three, and included a larger number of younger individuals than was found in the first group. The proportion of normal radiographs was equal in the two groups and so was the proportion of developmental changes (healed vertebral epiphysitis, osteochondritis and accompanying calcification in the anterior spinal ligaments). Changes in the intervertebral disks, other than the lumbo-sacral disk, consisting of slight narrowing or herniation of the nucleus into the adjoining vertebral body occurred with equal frequency in both groups. Lumbo-sacral anomalies were noted in 48.5 per cent of both groups. Asymmetrical lumbo-sacral facets and sacralization of the fifth lumbar vertebra occurred with slightly greater frequency in the backache cases. More combined anomalies occurred in the backache group. Sacralization and lumbarization were observed almost exclusively in females. No relation was noted between lumbo-sacral anomalies and radiating pain. Hypertrophic arthritis was present in 57 per cent of the backache group and in 25.7 per cent of the control group, that is it was twice as common in people complaining of pain in the back. On the other hand this group included a higher proportion of people over fifty years of age than did the control group. Scoliosis and increased lumbar lordosis were, similarly, twice as common in the backache group; decreased lumbar lordosis with flattening of the normal curve was six times as common. Spondylolisthesis was seen once in the backache group and slight forward slipping without any defect in the neural arch occurred once in the control group. In the sixty-two cases of backache in which a clinical diagnosis could be made there was not any correlation apparent between the diagnosis and the area which in the plates showed the greatest abnormality. The comparative numbers of plates showing dorso-lumbar changes were thirty-one in the backache and ten in the control group. Plates showing dorsal changes numbered thirty-two and eight respectively; showing lumbar changes, forty-five and six. Multiple areas of involvement were seen three times as often in the backache as in the control group. Lumbo-sacral changes other than structural anomalies occurred four and a half times as often in the backache group. Sacro-iliac changes were present in six of the backache cases and in none of the controls. Narrow posterior measurement of the lumbo-sacral disk was noted in 20.6 per cent of the backache group and 5.7 per cent of the controls. Posterior displacement of the fifth lumbar vertebra occurred in four of the backache group.

Review of sciatic pain conditions

Aetiology, diagnosis and treatment — The diagnosis and treatment of sciatic pain is discussed by R. I. Stirling in his Honyman Gillespie lecture. He divides cases into three groups. (1) Patients with some disturbance in the joints of the lower end of the spine or in the pelvis, and with referred pain along the sciatic nerve. Sensory or motor changes cannot be demonstrated. These are not cases of true sciatica. Most cases are due to derangement of one of the sacro-iliac joints, some to derangement of the lumbo-sacral joint and a few to derangement of the joint between the fourth and fifth lumbar vertebrae. Traumatic or postural strain is the commonest cause. The differential diagnosis between lumbo-sacral and sacro-iliac referred pain is made by moving the respective joints. If the sacro-iliac joint is affected, the patient when standing feels pain on attempting to touch his toes while keeping the knees straight; when sitting he is able to touch his toes without feeling any pain, when recumbent he feels pain in the affected joint when he raises the leg, with extended knee, on either the affected side or the opposite side. When the disturbance is in the lumbo-sacral joint this joint is held rigid when the patient attempts to touch his toes whether he is in the standing or in the sitting position. Straight leg raising in the recumbent position causes referred pain. (2) Pain results from some disturbance of the nerve or its roots. Sensory or motor abnormalities are noted. The chief causes are arthritis of the sacro-iliac or lumbo-sacral joints, infection or growth in the neighbourhood of these joints, sacralization of the fifth lumbar vertebra, spondylolisthesis, prolapse of an intervertebral disk or thickening of the ligamentum flavum, radiculitis, inflammation or growth inside or outside the spinal canal, and fibrositis. In radiculitis and protrusion of the disk the cerebrospinal fluid may show increased protein, and in the former it may show increase of cells. Intraspinal tumours may be associated with a positive Queckenstedt test. Radiography is essential. Aerography of the spinal canal usually gives disappointing results in the lower regions of the spine. (3) 'True sciatica' is usually associated with an infective focus somewhere in the body, and this focus must be sought and eliminated. Occasionally metallic poisoning or a metabolic anomaly may be the cause. Treatment is as follows. In the first group, manipulation is usually successful, with subsequent rest in bed followed by exercises. In the second group, treatment is that of the cause. In the third group, rest and then physiotherapy are necessary. Stretching of the nerve under an anaesthetic may also be helpful.

Sciatica caused by vertebral disk defect

Clinical picture and diagnosis.—J. E. A. O'Connell discusses the diagnosis of sciatica associated with protrusion of the disk between the fourth and fifth lumbar vertebrae or between the fifth lumbar vertebra and the sacrum. Clinical examination yields far more reliable results than does contrast radiography. Two types of clinical picture are seen. (1)

Rarely are the phenomena those of a severe cauda equina lesion with paralysis, sensory loss and sphincter disturbances. Recovery after removal of the prolapsed disk is often very slow and sometimes incomplete. (2) In most cases the picture is less striking. More than half the number of patients, of whom the majority are men, give a history of antecedent trauma. The pain, which characteristically occurs in attacks with intervals of complete or partial relief, usually begins in the lumbo-sacral region and runs down the leg in the distribution of the sciatic nerve. Occasionally backache is absent or only part of the sciatic distribution is involved. The pain is aggravated by exercise, coughing or straining. It is usually relieved by rest but sometimes wakes the patient at night and then it may be relieved when the patient walks about. Change of posture may relieve the pain. The reason appears to be that the pain results from stretching of the extradural parts of the nerve roots, which lie closely applied to the bodies of the vertebrae. Paraesthesiae are often complained of. On examination of the patient, tenderness and deformity (obliteration of the lumbar curve or actual lumbar kyphosis or scoliosis) are noted. The straight leg raising test causes pain on the affected side whichever leg is tested, but the sound leg can be raised to a more acute angle than the affected leg before pain is felt. The author describes a further step in this test by which both legs are raised together. Pain is not experienced until the angle is increased beyond that to which either leg alone can be painlessly raised. If the sound leg is then lowered, pain and paraesthesia are felt. Tenderness along the sciatic nerve is often present. Although actual paralysis is rare, atrophy, hypotonia and sometimes fibrillation are seen in some of the muscles supplied by the lower lumbar and upper sacral roots on the affected side. Sensory defects are often found. Absence of the ankle jerk on the affected side is common. The knee jerk is normal or increased. X-rays should always be taken to exclude osseous disease; they sometimes confirm the diagnosis by showing narrowing of the intervertebral space.

Treatment

Procaine in the Forces

Experience of sciatica in the Forces, as is pointed out in a Leading Article in the *Lancet*, shows that clinical traditions are fallacious. The idea that the disease is self-limited and only occasionally recurrent has been disproved. In patients in the Forces it shows a considerable tendency to chronicity, leading to much invalidism and in some cases to neurosis. An army bulletin recommends that, except in the most trivial cases, patients should be admitted to hospital for thorough examination. Fibrositis associated with trauma, postural strain or congenital bony anomalies is a common cause of sciatic pain; it has been estimated that 70 per cent of cases originate in this way. In such cases disturbance of sensation or of tendon reflexes in the legs cannot be detected. Deeply seated fibrositic lesions may require the exploring needle to locate them. Patients with fibrositis respond to infiltration with procaine; when the lesion is inaccessible, manipulation may succeed. Sciatica due to neuritis or radiculitis is associated with slight sensory impairment, a diminished or absent ankle jerk and occasionally weakness of dorsiflexion. In radiculitis the cerebrospinal fluid may show an excess of protein and lymphocytes. Chronic neuritis may respond to perineural injection of procaine, and radiculitis to epidural injections of procaine followed by normal saline. In sciatica due to prolapsed intervertebral disk a history of trauma is often given. Scoliosis, tenderness of the nerve and of the hamstrings and calf muscles, weakness of plantar flexion and dorsiflexion, and diminished or absent ankle jerk are common signs. Sensation is diminished on the outer side of the leg and on one side of the foot, with loss of postural sensation in the corresponding toes. Operation has proved so unsuccessful that patients in the Forces should be invalided if immobilization fails. Rarer causes are spinal disease, pelvic tumours and tumours of the cauda equina.

Soldiers' sciatica

Infiltration of tender spots with procaine.—M. G. Good has seen in the Army sixty-five patients with the syndrome of sciatica. The pain in all these patients was thought to be muscular in origin. Well defined myalgic spots, harder than the surrounding muscle, could be found in the quadratus lumborum, glutei or tensor fasciae femoris muscles. Pressure on these produced severe pain, sometimes similar in character and distribution to the sciatica complained of, and lasting for some minutes. Immediate and permanent relief was given in all but one of the cases by infiltrating each tender spot with 1 per cent procaine solution. In the one patient not cured it was discovered on psychological investigation that the pain was simulated. Care must be taken to map out the myalgic spots carefully beforehand on the skin with a blue pencil and to infiltrate each thoroughly, 1 to 2 cubic centimetres of solution usually suffice. The advantages of this treatment are its simplicity and rapidity.

Laminectomy

Iodized oil used in diagnosis.—O. R. Hyndman, A. Steindler and J. Wolkin describe sixty-three cases of sciatica in which laminectomy was performed for supposed herniation of an intervertebral disk and in which contrast radiography with iodized oil had been used as an aid to diagnosis. Herniated disks were found in fifty-three of the patients. The authors are not in favour of using iodized oil in every instance. It is usually unnecessary and should be kept for doubtful cases. There were not any complications after its use in this series. It may reveal multiple herniated disks; in four of the cases under review (9 per cent) herniation of both the fourth and fifth lumbar disks was present. Not less than 5 cubic centimetres of oil should be injected at the second lumbar interspace. Smaller amounts do not fill out the cul-

de-sac sufficiently. The column of oil as seen in the plate shows paired projections ('axillary pouches') at its margins marking the points at which nerves leave the spinal canal. In cases of herniated disk a filling defect is observed which in the authors' experience always includes or distorts the axillary pouch. The results of examination were: positive X-ray and herniated disk found in forty-six cases; positive X-ray and herniated disk absent in five of the early cases, in which it is thought that the lesion was present but was overlooked; negative X-ray and herniated disk found in one case; negative X-ray and herniated disk not found in three cases; false filling defects and herniated disk not found in five cases. The five patients concerned in last-named cases were completely relieved by the operation, at which either the appropriate intervertebral canals were partially unroofed or the sensory root cut. In cases of sciatic pain due to myofascial trauma 'trigger points' can often be found and pain can be abolished by infiltrating such points with procaine. Herniated disk is thus ruled out.

Surgical treatment

Removal of intervertebral disk and subsequent bone grafting.—At the Mayo Clinic a combined operation for low back and sciatic pain has been performed on 139 patients. It consists in exploration of the spinal canal for a prolapsed intervertebral disk, with removal if found, and subsequent bone grafting. The results are presented by R. K. Ghormley, J. G. Love and H. H. Young in a paper read at the annual session of the American Medical Association. Patients selected for the combined operation are those whose symptoms are relieved by rest but recur on resumption of activity and in whom some evidence of instability of the lumbosacral spine can be detected. All the patients included in this series were observed for at least a year, and some of them for three or four years. In seventy-seven a protruded disk was found and dealt with; in sixty-two a protruded disk was not found. A tibial graft was used in most cases. This saves time because it can be cut by the orthopaedic surgeon while the neurosurgeon performs the intraspinal part of the operation. The result was classed as 'good' when the pain was completely relieved and the patient was able to return to his former work, as 'fair' when pain was better but not completely relieved, and as 'poor' when there was not any improvement. Among the seventy-seven patients with protruded disk the result was good in forty-six, fair in eighteen and poor in eight; five were not traced. Among the sixty-two without protruded disk the result was good in forty-one, fair in fifteen, poor in three, three were not traced. Among the fair and poor results in both groups there were ten in which the graft was inadequate (too short, fractured and so on), one in which infection supervened, three cases of psychoneurosis, and three cases in which compensation claims are still unsettled.

EDITORIAL COMMENTARY—A General Summing up on Sciatica

Two principal factors have caused sciatica to be responsible for much invalidity in war service exposure, often due to sleeping in the open on damp ground, physical strain. The former has given rise to fibrositis of the lumbar and gluteal regions with pain referred to the distribution of the sciatic nerve, and this form was investigated by T. Lewis (1938) and J. H. Kellgren (1938) before the present war. As a result of their work treatment by injection of procaine in saline into the local thickenings and nodules in the muscles and aponeuroses in these regions has been widely used and found to be of great service. A solution of quinine urea hydrochloride, similarly administered, has also been found effective and has the advantage of being antiseptic. The effect is primarily analgesic but if a sufficient quantity is injected—not less than 5 cubic centimetres and much larger quantities may often be used with advantage—the effect is also mechanical, opening up the tissue spaces and breaking down newly formed adhesions. The analgesic effect, although lasting for several hours, is temporary and should be followed by massage and gentle manipulations to break up the nodules and thickenings in the muscles and fasciae. Local heat is a useful adjunct to this type of treatment. The usual practice is to make the injection into the tender spot or spots, but Good advocates examination for points at which pressure causes wincing—often an involuntary movement—and sometimes severe pain in the area of referred pain. These points he terms myalgic spots, and he finds them at the origin, insertion, along the edge of, or in the course of, a muscle. Although the more usual practice is to inject the tender nodules, in some cases a method which may be found more effective and which should certainly be tried is to search for the myalgic spots and inject there.

When physical strain appears to be the cause, the lesion may be a strain of the sacro-iliac or lumbosacral articulations, a prolapse of the nucleus pulposus of the intervertebral disk between the fourth and fifth lumbar vertebrae or the fifth lumbar vertebra and the sacrum; or some congenital defect of the lower spine may be brought to light. Stirling has discussed these conditions from the orthopaedic standpoint and puts forward a useful practical classification dividing sciaticas into (1) those due to referred pain, (2) those due to pressure on the nerve root, (3) those due to true interstitial neuritis which, as he points out, is the least common and probably does not account for more than 5 per cent of the cases. In cases of lumbosacral or sacro-iliac strain patients may benefit from suitable manipulation but this must always be based on an accurate understanding of the underlying condition, and the movements must only be such as are likely to lead to correction of any slight degree of subluxation or to relaxation of muscle spasm. A mere ritual of forced movements in all directions may easily do more harm than good. Rest is important whether manipulation is carried out or not; weight extension which permits some change of position may be effective,

or a plaster spica may be necessary. X-ray examination is desirable and should always include an oblique view, as well as the usual antero-posterior and lateral aspects, as this will give a better view of the foramina and the apophyseal joints; the cause may lie in either.

Prolapse of the nucleus pulposus has come into prominence in recent years as a cause of obstinate sciatica, and operation for its relief has been successfully carried out. The subject has been fully discussed in both British and American literature; in a recent article (Ghormley, Love and Young) the advantage of combining the operation for the removal of the prolapsed disk with some form of spinal fusion is strongly advocated to lessen the risk of recurrence from further protrusion. In the discussion on this paper it is wisely pointed out that there is plenty of room in the spinal canal at the level of the fourth and fifth lumbar vertebrae for the cauda equina and that a prolapsed disk may cause symptoms only if it protrudes in the vicinity of the foramen. In cases due to this cause there may be an acute onset followed by gradual subsidence of the symptoms and apparent cure, but a fresh attack occurs when some slight strain causes further protrusion and encroachment on the nerve roots. Therefore even if there is strong reason to suspect disk prolapse as the cause in an attack of sciatica it does not appear justifiable to operate until rest has had a good trial. Thickening of the ligamenta flava may also cause pressure on the nerve roots and attacks due to this are less likely to clear up completely, while fibrositis of the nerve sheath at the point at which it passes through the foramen, and displacement of the superior articular process from thinning of the disk or other cause may be a further cause of severe and obstinate sciatic pain.—C. W. BUCKLEY.

Brav, E. A., Bruck, S., and Fruchter, J. M. (1942) *Amer. J. Roentgenol.*, **48**, 39.
Ghormley, R. K., Love, J. G., and Young, H. H. (1942) *J. Amer. med. Ass.*, **120**, 1171.

Good, M. G. (1942) *Lancet*, **2**, 597.

Hyndman, O. R., Steindler, A., and Wolkin, J. (1943) *J. Amer. med. Ass.*, **121**, 390.

Kellgren, J. H. (1938) *Brit. med. J.*, **1**, 325.

Leading Article (1942) *Lancet*, **2**, 701.

Lewis, T. (1938) *Brit. med. J.*, **1**, 321.

O'Connell, J. F. A. (1943) *Brit. J. Surg.*, **30**, 315.

Stirling, R. I. (1943) *Edinb. med. J.*, **50**, 155.

SCLERODERMIA

See also B.E.M.P., Vol. XI, p. 37, and Cumulative Supplement Key No. 1390

Clinical types

Four forms of dermatosclerosis

Ætiological, diagnostic and therapeutic factors.—Under the inclusive title of 'dermatosclerosis' four diseases are considered by P. A. O'Leary of the Section of Dermatology and Syphilology of the Mayo Clinic. The diseases are grouped together in a differentially diagnostic sketch of scleroedema adultorum, scleroderma, acrosclerosis and dermatomyositis. These four forms of disease all present certain periods or phases, in the course of which the clinical manifestations are such as to create confusion and considerable difficulty in classification by the inclusion of manifestations characteristic of the other diseases under discussion. Thus thickening of the skin may be present in all the diseases at some stage or other. Implication of the muscular system has been responsible for the inclusion of the term dermatomyositis. Among the ætiological factors attention has been directed to infection, neurovascular involvement, arsenic and diffuse collagen disease. In addition to solid oedema and sclerosis of the skin, there are other factors which are common in these four diseases: in many of the cases there is a tendency for the disease to be self-limited, the oedema as it passes off being followed by atrophy and residual pigmentation. The four diseases are usually difficult to distinguish in their early stages because the cutaneous or solid or non-pitting oedema is common to all forms, similarly when the diseases are well established and frank the differential diagnosis is easier. The four diseases are separately summarized. Scleroedema adultorum usually comes on up to six weeks after an acute infection, such as acute streptococcal infection, influenza, tonsillitis or scarlet fever; the cutis is mainly inflamed and the muscular tissue escapes. The patches of inflamed skin, often on the sides of the neck, cannot be picked up in folds; the patient looks as if he had been poured into the skin of his neck and trunk, the hands and feet escaping oedema. Scleroedema tends to undergo spontaneous involution in from three months to a year but the course may be prolonged, relapses are not rare. Specific treatment is not known, but O'Leary believes that the use of foreign protein therapy in the form of typhoid vaccine is of value. Scleroderma is the most frequent of the four forms of the diseases concerned, and may be either generalized or localized (morphoea). When the fingers become sclerodermatous, the condition is called sclerodactylia. The onset of the generalized form may be gradual and insidious, or the disease may come on with oedema and so is indistinguishable from scleroedema adultorum. The term acrosclerosis was applied by J. Seller to a form of scleroderma with vasospastic involvement of the extremities and was long before discussed by Raynaud. The morbid changes are the same as those in diffuse scleroderma. Dermatomyositis has the marks of an infection. The dermatoscleroses are all treated empirically and symptomatically.

O'Leary, P. A. (1943) *Canad. med. Ass. J.*, **48**, 410.

SEBORRHOEA AND SEBORRHOEIC DERMATITIS

See also B.E.M.P., Vol. XI, p. 55.

Seborrhoeic dermatitis and the seborrhoeides**Treatment**

Liver extract and vitamin B.—A. Sayer defines seborrhoea as a dysfunction of the oil-secreting glands of the skin. The fact that seborrhoeic dermatoses are commonly associated with anaemia, with dyspepsia and with debility points to a general cause, and it is considered that this cause is deficiency of vitamin B. The micro-organisms, for example Unna's bottle bacillus, which have been noted in the lesions, would be on this basis secondary invaders. Seborrhoeic dermatoses are apt to be extremely resistant to local applications; on the other hand many workers have reported good results from the administration of the various components of the vitamin B complex, especially riboflavin. The author has treated a number of patients by injections of liver extract and by diets rich in vitamin B, and has found such treatment highly effective.

Sayer, A. (1942) *Urol. cutan. Rev.*, **46**, 719.

SENESCENCE AND SENILITY

See also B.E.M.P., Vol. XI, p. 69; and Cumulative Supplement, Key No. 1394.

Normal old age**Generalized atrophy**

Rules for longevity—The physiological changes of old age are considered by A. J. Carlson as they affect the following organs and tissues. (1) Bone, teeth and cartilage. The bones show gradual demineralization and increased brittleness, possibly due to a change in the chemical combination of the bone calcium. The red bone marrow of the vertebrae diminishes in quantity and the lecithin of the bone marrow is reduced. In the teeth reduced permeability of the enamel, thickening of the secondary dentine and increase of calcium content have been described. In cartilage atrophic and regenerative changes are seen side by side. (2) The lymphatic system. Evidence has been obtained of atrophy and fatty infiltration of the lymph nodes. Some decrease occurs in the lymphatic tissue of the appendix, spleen, tonsils and adenoids. (3) The blood. The fragility of the erythrocytes has been reported to increase with advancing age, otherwise the blood is unaffected. (4) The skin shows loss of fat, water and elasticity with decrease of growing and regenerating power. Skin wounds are said to take about five times longer to heal in a person of sixty than in a child of ten. The sebaceous glands tend to hypertrophy. The author further considers the proper diet for old age, emphasizing the importance of cutting down the quantity of food taken. Obesity is a factor tending to shorten life and its prevention in all people over thirty should contribute to longevity. In some cases disorders of the endocrine system may be to blame, but in many cases the chief reason for increasing weight seems to be that the ageing person continues to take food in excess of his diminishing energy requirements. In all types of obese people the weight can be reduced by cutting down the intake of food sufficiently. The reason why fat people tend to die early is obscure.

Senile deafness

Pure and mixed forms—L. Colledge remarks that senile deafness is merely a further stage of the lowering of the upper tone limit which is an almost universal concomitant of advancing age. When this lowering comes to include those tones used in ordinary speech symptomatic deafness results. The only aetiological factors known are familial predisposition and exposure to gunfire, as exemplified in the premature senile deafness of which many cases have been seen in men who fought in the war of 1914-18. Lowering of the upper tone limit may be due to atrophic changes in the ligamentum spirale, the function of which is most important in the lower whorl of the cochlea. The basilar membrane would thus lose its tension and high notes would be heard less well. The real deafness of old age has been attributed to atrophy of the auditory nerve with degeneration of the myelin sheaths and loss of insulation between the fibres. Pure senile deafness is not associated with any other symptom. The complaint almost always is that although conversation can be carried on with one person, general conversation is impossible because a voice becomes confused and lost in the general noise. Mixed forms of deafness are, however, frequent; and it may be possible to improve such cases by treatment of the middle ear or pharyngeal (Eustachian) tube. In the presence of tinnitus or vertigo other factors, including tobacco, tea and coffee, dental sepsis and arteriosclerosis may be reinforcing the senile changes. No treatment is of any avail for pure senile deafness, whether to arrest or to cure. Much help can be given by a suitable hearing aid, especially by one incorporating the thermionic valve. The aim is to amplify the upper more than the lower tones. The possibility of inflammatory or neoplastic disease of the auditory apparatus must be remembered.

Carlson, A. J. (1943) *Northw. Med., Seattle*, **42**, 46.

Colledge, L. (1943) *Practitioner*, **150**, 335.

SEPTICAEMIA AND BACTERIAEMIA

See also B.E.M.P., Vol. XI, p. 76; and Cumulative Supplement, Key No. 1395.

Clinical consequences of a bacteraemia

Affections of the eyes

Investigation of primary foci.—The present position of focal infection in ophthalmology is critically examined by A. C. Woods. When first propounded, the theory of focal sepsis resulting in intermittent transient bacillaemia was immediately accepted by many without question and much indiscriminate surgery ensued. Brilliant results were claimed in various diseases for the removal of teeth and tonsils and for various other procedures. Less credulous observers, however, were soon pointing out that the patient was often no better and sometimes even worse after the eradication of the suspected source of infection. Attempts to develop laboratory procedures to determine the relation between the primary focus and its supposed result were in the main unsuccessful. The author believes that foci of infection should still be sought for in cases of ocular disease and if they are believed to be of importance should be removed. The routine removal of minor and symptomless foci of infection has no place in ophthalmology.

Staphylococcal bacteraemia and septicaemia

Treatment

Successful results with penicillin.—During 1941-2, Dorothy H. Heilman and W. F. Herrell largely confirmed the results of the Oxford workers, and compared the action of penicillin with that of another antibiotic agent, gramicidin, both being found to be of the same order of activity against Gram positive cocci, although there are decided differences in the selective bacterial activity of the two agents. Penicillin without being haemolytic is superior in the possession of bacteriolytic power as regards some micro-organisms. Bactericidal amounts of penicillin may be given locally or subcutaneously without evidence of toxicity. Penicillin-containing pyogens may induce fever if given intravenously, but intravenous injection of pyrogen-free penicillin can be given without causing fever. On the basis of present evidence it appears that penicillin should be most useful in the treatment of infections by *Staphylococcus aureus*, *Streptococcus pyogenes*, *Diplococcus pneumoniae*, *Neisseria gonorrhoeae*, *N. intracellularis* and bacteria associated with gangrene; the British observers state that the bacteria classed as *Streptococcus viridans* were resistant to penicillin. *Actinomyces bovis* is susceptible to penicillin, whereas *B. tuberculosis* is not so. The above workers, together with H. I. Williams, report a case of severe staphylococcal infection successfully treated with penicillin. A man aged thirty-three was admitted to hospital after a four days' illness beginning with soreness inside the right nostril. He had previously suffered from boils, the last appearing about a year before. Examination disclosed cellulitis of the nose with great oedema of the right side of the face and neck. The right eye was displaced downwards and outwards and its movements greatly limited. The temperature was 104° F. Cultures from the nose and blood grew *Staphylococcus aureus*. During the first thirty-six hours a total of 18.6 grammes of sulphadiazine was given, but when the pathological report was received, and as the patient was getting worse, penicillin was substituted. Blood culture taken just before it was begun was still positive. A total of 160,000 Oxford units was given in a continuous intravenous saline drip during the next nine days. Blood culture twenty-two hours after the drip was started was sterile and the patient made a good recovery. No toxic manifestations were noted. The writers consider the intravenous drip to be the best method of maintaining a constant adequate concentration in the blood.

Streptococcal bacteraemia and septicaemia

Streptococcus viridans

Relief after ligation of patent ductus arteriosus.—O. S. Tubbs records the case of a woman, aged twenty-two years, with a history of about four months of right-sided pleurisy. When she was first seen the temperature was 103.6° F., systolic and diastolic murmurs were audible in the pulmonary area, blood culture was positive for *Streptococcus viridans*, which rapidly became negative after ligation of the patent ductus arteriosus. The patient made a complete recovery from a left-sided pleurisy which appeared on the fifth post-operative day. F. P. Weber regarded the patent ductus arteriosus, just as a congenital valvular malformation or the scar from an old rheumatic endocardial lesion would be, as a place of less resistance toward any streptococci which might happen to be in the blood stream. He suggested that the reason for the rapid disappearance of the *S. viridans* from the blood stream was that the ligation, by closing up this surface of imperfect endothelium, deprived the streptococci of their breeding ground, or of most of it.

Treatment

Influence of pantothenic acid.—H. McIlwain and F. Hawking find that the growth of haemolytic streptococci depends upon a factor, pantothenate, which is present in the host's blood. They reason that by preventing the organism from obtaining this substance its growth could be inhibited. In the case of sulphanilamide it has been shown that the latter acts by antagonizing a substance, *p*-aminobenzoate, to which it is chemically related. Pantothenate is structurally similar to pantoic acid and the latter was therefore selected for trial. It was found that *in vitro* the growth of haemolytic streptococci depended upon the relative concentration of pantoic acid and pantothenate in the medium, and was inhibited when the ratio was increased above a certain point. *In vivo* the action of pantoic acid was similar, but care was necessary to adjust the dose according to the amount of pantothenate normally present in the blood of the experimental animal. Thus pantoic acid was found to be inactive against

haemolytic streptococci in mice, which have a high blood pantothenate level, but to prevent death from infection in rats, in which the blood pantothenate is comparatively low. Rats treated with 25 per cent solution of the 90 per cent pure sodium salt of pantooyltaurine for four days were protected against 10,000 lethal doses of virulent streptococci. When the blood pantothenate level of the rats was artificially raised pantooyltaurine did not have any effect. As pantooyltaurine was rapidly excreted in the urine frequent hypodermic doses were necessary to maintain a sufficient concentration in the blood. Pantooyltaurine is thought to act by blocking the pantothenate at some point and preventing it from being utilized by the organism. Sulphonamide-resistant strains of streptococci and some strains of *Corynebacterium diphtheriae* were found to be sensitive to pantooyltaurine. The growth of pneumococci was slightly inhibited. Staphylococci, *Bacterium coli*, *B. proteus*, *Trypanosoma equiperdum* and *Plasmodium relictum* were unaffected.

Heilman, Dorothy H., and Herrell, W. E. (1942) *Proc. Mayo Clin.*, **17**, 321.

Herrell, W. E., Heilman, Dorothy H., and Williams, H. L. (1942) *Proc. Mayo Clin.*, **17**, 609.

McIlwain, H., and Hawking, F. (1943) *Lancet*, **1**, 449.

Tubbs, O. S. (1943) *Proc. R. Soc. Med.*, **36**, 175.

Weber, F. P. (1943) *Proc. R. Soc. Med.*, **36**, 176.

Woods, A. C. (1942) *Amer. J. Ophthalm.*, **25**, 1423.

SEX HORMONES

See also B.E.M.P., Vol. XI, p. 90; and Cumulative Supplement, Key Nos. 1396–1398.

Source and constitution

Male sex hormone

General review of chemistry—G. J. Newerla sketches the history of the discovery and isolation of the male hormones. Testicular tissue was recommended for impotence in 1400 B.C. but the first scientific proof of its effects was provided by the experiments of Berthold who in 1848 showed that transplantation of cocks' testes into capons was followed by development of the comb and wattles and of the fighting and reproductive instincts. In 1889 E. Brown-Sequard revived interest in the subject by claiming rejuvenating powers for aqueous extracts of testicular substance. The study of testicular function advanced slowly. Interrelations with other glands were demonstrated. Transplantation experiments were carried out in large numbers. Ligation of the vas deferens was tried, on the hypothesis that atrophy of the seminiferous epithelium would be followed by hypertrophy of the interstitial cells. Most of this experimental work had rejuvenation as its avowed aim. In 1926 came a considerable step forward in the preparation by McGee of a lipid extract of bulls' testes of which 0.01 milligram would restore the atrophic comb of a capon. Three years later S. Loewe and H. E. Voss reported that an extract made from normal men's urine would reverse the effects of castration in the mouse. In 1931 A. Butenandt succeeded in isolating in crystalline form two chemically pure substances, androstosterone and dehydroandrostosterone, from men's urine. He found that they were sterols closely related to the female hormone oestrone, and he assigned to them chemical formulae. L. Ruzicka and his associates shortly afterwards produced androsterone synthetically. In 1935 testosterone, many times more potent than androsterone from which it differed slightly in chemical formula, was isolated by K. David. Up to the present time more than thirty substances with male hormone properties have been prepared synthetically. They are sterols related to those found in bile, adrenal cortex and other substances and to some vitamins and to the carcinogens.

Hepatic inactivation of testosterone and methyl testosterone.—M. W. Burrill and R. R. Greene have investigated the inactivating effect of the liver on testosterone and methyl testosterone in rats. Pellets of the hormones were implanted into the mesentery or spleen of castrated male rats. Eleven days later the rats were killed, the ventral prostate glands and seminal vesicles were removed and weighed, and the pellets were recovered, dried and weighed. As a control, in another group of rats the pellets were implanted subcutaneously. The weights of the accessory organs, compared with those of castrated controls, were taken as an index of effectiveness of the implants. Both testosterone and methyl testosterone proved effective when implanted subcutaneously so that the hormone was absorbed directly into the systemic circulation. When implanted in the spleen, so that the hormone was carried in the portal system to the liver, methyl testosterone had some effect, testosterone had none. When implanted in the mesentery both were moderately effective, possibly because of partial absorption into the circulation via the lymph stream without passage through the liver. Oral administration, therefore, assuming that absorption takes place through the portal system, should be less effective than subcutaneous administration, although it is of some value when methyl testosterone is used.

Use of sex hormones in treatment of menstrual and climacteric disorders

Preparations and standardization of female sex hormones and gonadotrophic hormones

Stilboestrol, stilboestrol dipropionate and stilboestrol dipalmitate.—S. C. Freed, W. M. Eisin and J. P. Greenhill have compared the therapeutic efficiency of stilboestrol, stilboestrol dipropionate and stilboestrol dipalmitate, using as a criterion the subjective response in meno-

pausal subjects. They argue that the use of animals for assay gives results that are unreliable and are often conflicting; that endometrial biopsy is an awkward method, the accuracy of which is diminished by the fact that endometrial appearances vary in untreated menopausal women; and that vaginal smears also show varying degrees of cornification at the time of the menopause. The method used by the authors was to give an injection of the compound to be tested once a week for three weeks. The dose given was 5 milligrams of stilboestrol or the calculated equivalent of one of the other compounds. After the third injection the patients were seen at intervals of two or three weeks and placebo injections were given to minimize the effect of suggestion. The dipalmitate compound was found to be far more effective than was either of the other compounds, the relief produced by it lasting for an average of from nine to ten weeks and only 11.6 per cent of patients failing to obtain less than five weeks' relief, as compared with 43.9 per cent on the dipropionate and 65.6 per cent on stilboestrol. The dipalmitate derivative was also much less toxic; nausea, with or without other symptoms, occurred in 46.8 per cent of patients treated by stilboestrol, in 14.6 per cent treated by the dipropionate and in 2.3 per cent treated by the dipalmitate. The reduced toxicity probably results from the lower rate of absorption of stilboestrol dipalmitate.

Mode of administration and dosage

Cyclical oestrogen therapy.—A Palmer has investigated the possibilities of cyclical oestrogen therapy. The uninterrupted administration of oestrogenic substances to rats and mice over periods of weeks or months has given rise to a variety of ill effects and there is a danger that, with the introduction of stilboestrol, which is both cheaper and more potent than were earlier preparations, the injudicious therapeutic use of oestrogens may lead to similar results in human beings. For treating menopausal symptoms the author has found that cyclical hormone feeding is effective and economical. A cycle of treatment should consist of three weeks' daily administration, with one week's rest afterwards. The daily dose recommended is from 0.2 to 0.5 milligram of stilboestrol, on which the urinary excretion of oestrogen has been found to approach that of the non-menopausal woman. If the hormone cannot be tolerated when given by mouth it may be given by injection, preferably in the form of an oestrogen ester; the dose recommended is from 0.1 to 1.0 milligram at weekly intervals. The effect of oestrogen esters is more protracted than is that of the oestrogens themselves. For young women with hypo-ovarian amenorrhoea or with primary hypogonadism, the recommended dose of stilboestrol is 1 milligram daily for seven days and then 5 milligrams daily for seven days. Treatment is then stopped and the sudden fall from a high to a low level of circulating hormone may be expected to result in a 'period'. An interval of fourteen days is allowed to elapse before oestrogen administration is begun again, so that the cycle of treatment lasts twenty-eight days.

Burrill, M. W., and Greene, R. R. (1942) *Endocrinology*, **31**, 73.

Freed, S. C., Eisn, W. M., and Greenhill, J. P. (1942) *J. Amer. med. Ass.*, **119**, 1412.

Newerla G. J. (1943) *New Engl. J. Med.*, **228**, 39.

Palmer, A. (1942) *Amer. J. Obstet. Gynec.*, **44**, 56.

SHOCK AND COLLAPSE

See also B.E.M.P., Vol. XI, p. 126; and Cumulative Supplement, Key No. 1400.

Hypotheses of shock

Toxaemia

Effect of muscle extracts on the heart—In an endeavour to obtain evidence bearing on the relation between muscle injuries and shock, N. Pace and R. J. Main have investigated the effect of muscle extractives on the perfused heart. They used for the purpose Valentine's meat extract, which is prepared by extracting beef muscle with hot water and concentrating the fluid *in vacuo*. The frog heart preparation was perfused with Ringer's solution until the rate and amplitude of the beat were constant, this usually required from thirty to forty minutes. Ringer's solution containing various concentrations of meat extract was then substituted, and the effect was observed for at least an hour. For making the dilutions, except the highest ones, of the meat extract, potassium-free Ringer's solution was used because of the high potassium content of the extract itself. Normal Ringer's solution was then used for a further thirty minutes. The meat extract was found to produce a considerable increase in the amplitude of the heart's contractions, which was maintained for as long as perfusion by the extract was continued. This effect was seen with dilutions ranging from 0.56 to 0.05 per cent. In the stronger solutions the heart showed a tendency to stop in diastole, owing probably to the unavoidable excess of potassium in the perfusion fluid. A slight change in rate, usually slowing, was often observed. To obviate the possible effect of this change of rate upon the amplitude of the beat, a further series of experiments was carried out upon hearts driven by electrical stimulation at a constant rate. The positive inotropic effect of the meat extract was still apparent. When mammalian (guinea-pig) hearts were used for perfusion similar results were observed. The meat extract was then dialysed in a Cellophane tube for twelve hours, and the fluid inside and outside the tube was separately tested in equal dilution. The fluid outside the

tube was found to be much the more active, showing that the substance concerned is dialysable. Electrolysis of the extract showed that the active principle went to the anode when the extract was at pH 5.6. The principle was found to be slightly soluble in alcohol and insoluble in ether. Several pure compounds reported to be in the meat extract and having somewhat similar chemical properties were then tested separately, and both guanidine and creatine were found to exert an amplifying effect on the contractions. Guanidine is present in such minute quantities that it probably does not play any significant part. Creatine is present in a concentration sufficient to account in large part for the effect noted.

Haematogenic shock

Aetiology and treatment.—H. Devine states that the term shock is generally applied to acute circulatory failure developing soon after severe trauma or toxic injury. The circulatory disturbance is generally a complex of two conditions and may be divided into the following phases. (1) Neurogenic, comprising primary shock and shock associated with spinal anaesthesia or fainting; (2) haematogenic or secondary shock, in which reduced blood volume is the primary feature; (3) vasogenic, in which the effect is directly upon the blood vessels, and of which histamine shock is an example, (4) cardiogenic, in which the circulatory failure is central in origin. In neurogenic shock the vessels are dilated and the extremities are warm, and therefore vasoconstrictor drugs are useful in treatment. The aetiology of haematogenic shock has been much debated. Progressive reduction in the blood volume results in increasing anoxia of the tissues and haemoconcentration is the characteristic sign. Preventive measures include a diet rich in protein and adequate in fluid, this diet should be given to all soldiers who are going into battle. Temperance in the use of tourniquets should be practised. When haematogenic shock has developed, restoration of blood volume is the paramount consideration. When much blood has been lost, blood is the ideal fluid for transfusion but if blood cannot be obtained immediately plasma, serum, or even saline may be used in the meantime. In haematogenic shock plasma or serum should be given continuously until the haematocrit readings fall to normal; crystalloid solutions given intravenously not only fail to increase the blood volume permanently but also may even reduce it by carrying more protein out of the blood. In patients suffering from the crush syndrome renal damage should be forestalled, if possible, by applying a tourniquet to the crushed limb before it is released and by giving abundant fluids, in hospital the tourniquet is replaced by a sphygmomanometer cuff which is deflated slowly, the limb is kept cool with ice and diuretics and alkalis are given. Drugs are of little use in shock although cardiazol (leptazol), veritol (pholedrine) and sympatol are sometimes useful, and oxygen is of value.

Treatment

Desoxycorticosterone acetate

In post-operative shock.—The possibilities of desoxycorticosterone acetate and saline infusions in preventing and treating post-operative shock have been studied by H. Koster and L. P. Kasman in a series of 200 patients undergoing severe operations. A similar group of 200 patients was taken as a control, and the numbers for the various operative procedures were equal in the two groups. Spinal anaesthesia was used in all the cases. The dosage of desoxycorticosterone acetate was 5 milligrams twice daily for from one to four days before operation and for the next four days, and once daily afterwards until the fourteenth day; except in twelve acute cases, in which 5 cubic centimetres of cortical extract was given intramuscularly every six hours for the first forty-eight hours and 5 milligrams of desoxycorticosterone acetate twice daily for the next four days and once daily afterwards for from ten to fourteen days. All the patients received 1,000 cubic centimetres of saline and glucose (5 per cent) solution twice daily for four days after operation, and the non-urgent patients for several days before operation. The control group received only saline infusions. The mortality rate was 11 per cent in the treated group and 9 per cent in the untreated, indicating that cortical preparations are not of any value in the prevention and treatment of post-operative shock.

Oxygen

Treatment by high concentration.—G. Melton records results of administration of high concentrations of oxygen to shocked patients. Thirty-one cases of shock associated with various injuries and diseases were treated. In most cases the B. L. B. mask was used, with a flow of from 6 to 8 litres per minute. Administration was begun as soon as possible after the patient was admitted to hospital and as far as possible before any other treatment was given, so that the effects of the oxygen could be assessed. In each patient the effect of stopping the flow was also recorded. In most cases the changes appeared rapidly. Six of the patients did not show any response to oxygen or to its withdrawal. The remaining twenty-five all improved when oxygen was given and seventeen of them showed signs of relapse when it was stopped. Thirteen out of seventeen patients with bleeding which had been arrested improved with oxygen as compared with ten out of thirteen in whom loss of blood had not occurred, but improvement was more pronounced in the former group of cases. The chief effect of oxygen was a rise of both systolic and diastolic blood pressures. The effect on the pulse was inconstant; in some cases the rate was reduced, in others it was increased.

Devine, H. (1942) *Med. J. Aust.*, **2**, 19.

Koster, H., and Kasman, L. P. (1942) *Arch. Surg., Chicago*, **45**, 272.

Melton, G. (1943) *Lancet*, **1**, 481.

Pace, N., and Main, R. J. (1942) *J. Pharmacol.*, **75**, 283.

SILICOSIS

See also B.E.M.P., Vol. XI, p. 133; and Cumulative Supplement, Key No. 1401.

Aetiology**Industrial processes**

Bagassosis.—L. I. M. Castleden and J. L. Hamilton-Paterson describe under the title bagassosis (not bagasscosis, as it has been called) 'an industrial lung disease', due to the inhalation of dry bagasse (broken sugar-cane) dust, the fibre of which contains from 5 to 7 per cent of silica. In 1940, the process of preparation of bagasse was altered from being moist to being dry with much dust; directly after this change and the liberation of irritating dust, cases of respiratory disease among the workmen arose. When the significance of this sequence of events was realized measures were taken to prevent the occurrence of a dusty state of the atmosphere of the factory. Of the four cases, two were acute, and ran a course ending in cure. J. A. Gillison and F. Taylor observed four cases from the same factory, two of them being among the four patients reported on by Castleden and Hamilton-Paterson. The four cases were further investigated at the London Chest Hospital by F. G. Wood, H. V. Morlock and S. R. Gloyne.

Course and prognosis**Complications**

Tuberculosis P. M. Ellis, M. T. Smith, H. F. Bonebrake and L. B. Hunter report the results of a survey of silicosis cases in a group of miners in Idaho. Since 1935 a routine medical examination has been carried out of all new employees and of those already working in the mines, with further investigations (X-ray, sputum and Wassermann examinations) if such are considered necessary. About 10,000 men have been examined, and the results in 7,542 cases are described, of these 6,243 men had been exposed to silica dust, and in 1,299 there was not any history of exposure. The percentage of the total free from evidence of silicosis was 31. Silicosis alone was diagnosed in 67 per cent, tuberculosis without silicosis in 0.24 per cent and silicosis complicated by tuberculosis in 2.31 per cent. The disability from uncomplicated silicosis is not great, superimposed infection is mainly responsible for any symptoms. The most serious effect of silicosis is the increasing of susceptibility to tuberculosis. Prevention of silicosis is an important problem which must be solved by the engineer; various measures have been put into practice in the mines with such an aim in view. Prevention of tuberculosis is a medical problem. All employees should be examined frequently so that tuberculosis may be detected early, and the patients segregated and treated.

Castleden, L. I. M., and Hamilton-Paterson, J. L. (1942) *Brit. med. J.*, **2**, 478.

Ellis, P. M., Smith, M. T., Bonebrake, H. F., and Hunter, L. B. (1942) *Northw.*

Med., Seattle, **41**, 406.

Gillison, J. A., and Taylor, F. (1942) *Brit. med. J.*, **2**, 577

SKIN DISEASES: AFFECTIONS DUE TO INSECTS AND ACARINES

See also B.E.M.P., Vol. XI, p. 149, and Cumulative Supplement, Key Nos. 1403 and 1404.

Parasites breeding on human host***Acarus scabiei***

Scabies in children R. T. Brain discusses the problems of scabies in children. Diagnosis is often difficult. It is worth while in doubtful cases to examine the parent. A swab wetted with Dettol solution is used to cleanse the creases about the wrist and palm before they are examined for burrows. Confirmation of the diagnosis may be obtained by moistening the burrow with liquor potassae and scraping it out with a scalpel, when the microscope shows an ovum if not an acarus. The condition most likely to cause difficulty in diagnosis is urticaria. If an urticarial subject gets scabies an urticarial papule or vesicle develops which completely obscures the lesion. Eczema may be mistaken for scabies, and difficulty may arise when an extensive eczema masks an underlying scabies. Search should be made for burrows and for the minute scattered papules resulting from invasion of the follicles. Pediculosis may imitate the itching eruption of scabies but the skin lesions are more localized and larger than those of scabies. The complications of scabies include impetigo (the most common), eczema and urticaria. The scabies should be treated whether complications are present or not, and complications should be dealt with afterwards. A hot bath with thorough soaping is first given to soften the stratum corneum. The skin is rinsed and dried and an insecticide is applied to the whole body. In infants this includes the face and scalp; older children and adults may be treated from the neck downwards. A second treatment within eight days is advisable unless signs of intolerance appear. Benzyl benzoate emulsion (National War Formulary) is the preparation of choice, applied with a flat brush. The skin is dried by exposure in a warm room and clean clothes are put on. Clothing and bedclothes must be disinfected. Dermatitis rarely occurs when benzyl benzoate is used, but the drug may cause a burning sensation.

Treatment by emulsions.—K. C. Mallen has compared the effects of aqueous and spirit emulsions in a series of soldiers treated for scabies by benzyl benzoate. The aqueous emulsion was used in 448 cases, the spirit emulsion in 527. The proportion of benzyl benzoate to vehicle was the same in both preparations. All the men were treated as in-patients. A bath, followed by applications of benzyl benzoate, was given on two successive days. On the third morning

the patient was seen by the medical officer and was either given one treatment with calamine lotion and was discharged the next day or, if impetigo or some other secondary infection was present, he was transferred to another department for further treatment. Some patients were not cured by two applications; twenty-eight needed three treatments, three needed four. The results were as follows. The aqueous emulsion gave cures in 99.8 per cent of cases, with recurrences in 0.24 per cent and dermatitis in 3.1 per cent; the spirit emulsion gave cures in 98.4 per cent, with recurrences in 1.56 per cent and dermatitis in 1.2 per cent. Thus the aqueous emulsion appears to be superior in efficacy to the spirit emulsion, as well as being cheaper, but to carry a slightly greater risk of causing dermatitis.

Use of tetraethylthiuram monosulphide.—The results obtained in a series of 107 patients treated for scabies with tetraethylthiuram monosulphide (T.E.T.M.S.) are presented by T. M. Clayton. A preliminary test of the 25 per cent emulsion was made, in order to discover whether it was likely to cause dermatitis, by rubbing it into the skin of fifteen volunteers after scrubbing on three successive days. No untoward results following, the emulsion was then applied after the usual scrubbing to fourteen patients with severe scabies, complicated in thirteen by sepsis. Three to five applications were made. Ten cures were obtained. The remaining ninety-three patients, less severely affected, were treated with a 5 per cent aqueous solution. All were cured although six subsequently became reinfected. Mild dermatitis occurred in seven cases. The number of treatments varied from one to eight, with an average of three. No directions were given to sterilize clothing and other articles as this is considered unnecessary.

Braim, R. T. (1943) *Practitioner*, **150**, 231

Clayton, T. M. (1943) *Brit. med. J.*, **1**, 443

Mallen, K. C. (1942) *Brit. med. J.*, **2**, 452.

SKIN DISEASES: OCCUPATIONAL DISEASES

See also B.E.M.P., Vol. XI, p. 161

Dermatitis

Causes

Industrial dermatitis—Sibyl Horner introduced a discussion on industrial dermatitis at a meeting of the Section of Dermatology of the Royal Society of Medicine. Although dermatitis in industry is not now notifiable, the number of cases which are voluntarily reported to the Ministry of Labour and National Service has increased from 2,000 cases in 1938 to nearly 5,000 in 1940. Dermatitis and ulceration of the skin which are produced by dust or liquids are compensatable (by certificate from the examining surgeon) under the Workmen's Compensation Act, the number of such cases was 2,735 in 1938 and 6,196 in 1940. Preventive work in Great Britain has made important advances lately but much remains to be done in the way of effective supervision in factories. The workers have a lurking fear that dermatitis is due to dirt and that it is contagious. The result is a free use of soap and water and antiseptics, even when instructions are given to the contrary, and thus cure is delayed. The recognition of industrial dermatitis depends upon clinical observation and upon the accuracy of the clinical history. The patient should be asked to give his own opinion regarding the origin of the lesion and to demonstrate his movements when at work; friction alone or in combination with an irritant may sometimes be responsible. The common causes of industrial dermatitis at the present time are oil, chemicals (including explosives), alkalis, solvents or degreasing agents. Cleansers, often alkaline or degreasing in character, are sometimes more responsible for dermatitis than are the industrial materials which are being handled. Dusts, sprays and vapours usually affect the face, the exposed part of the neck and the flexures before they affect the hands. The prevention of industrial dermatitis includes selection of suitable staffs and workers, protection by splash guards and protective clothing and the use of a good non-irritant 'barrier substance'. Attention is directed to certain special forms of industrial disease of the skin. The use in industry of chlorinated naphthalene waxes gives rise to a characteristic skin lesion, a non-infective folliculitis, which is seen on the forearms in early cases but which occurs most typically on the malar and mental regions of the face. Pustulation may be present in late cases and occasionally there may be general systemic symptoms of malaise and depression, with digestive disorders. The cutaneous affection seems to be due to the actual deposition on the skin of vapour from the heated wax, rather than to internal absorption and subsequent excretion. Exposure to fumes during the heating of chlorinated naphthalene waxes has been followed by a few cases, some fatal, of serious hepatic disease. The skin reaction to chromic acid and to the bichromates may not be typical ulceration (which is notifiable), but may be some form of dermatitis which is indistinguishable from that caused by other irritants. Several forms of glue—some acid, others alkaline—which are used for aircraft, also cause dermatitis.

Horner, Sibyl (1942) *Proc. R. Soc. Med.*, **35**, 701.

SKIN DISEASES: TUMOURS

See also B.E.M.P., Vol. XI, p. 200; and Cumulative Supplement, Key Nos. 1412-1415.

Innocent tumours

Derived from superficial layers of epithelium

Characteristics and treatment of warts.—R. H. Rulison has made a statistical study of warts

in 872 persons (42·7 per cent males, 57·2 per cent females). They were of four types, namely ordinary warts (71·6 per cent), plantar warts (19·2 per cent), juvenile flat warts (6·5 per cent) and filiform warts (2·7 per cent). Because of their rarity acuminate warts were not included in the survey. In forty-nine of the cases further warts developed after periods which were sufficiently long to rule out the possibility of recurrence. The highest incidence was in patients in the age group of sixteen to twenty years; the lesions were multiple in all cases of juvenile flat warts, in 52·6 per cent of ordinary warts, in 42·1 per cent of plantar warts and in 50 per cent of filiform warts. It is suggested that multiple warts occur in persons having little or no natural immunity or in whom antibodies fail to develop. Warts tend to be refractory, although they may disappear spontaneously. Of the multifarious methods of treatment, ranging from magic to surgical excision, none is specific. Only 55 per cent of 748 patients who were treated by various methods were cured. Because of the likelihood of relapse, patients should be observed for at least six months before a cure is claimed.

Derived from sweat glands

Fox-Fordyce disease.—A case of Fox-Fordyce disease in a woman of twenty-five is reported by A. C. Roxburgh. Three weeks after marriage, two and one half years before, the patient developed irritation in both axillae and on the breasts, pubes and lower abdomen. The axillary and central pubic hair disappeared. The irritation was worse at night and after coitus and was not related to the menstrual periods, which had always been and continued to be prolonged and frequent. On examination she had numerous domed perifollicular papules in both axillae, extending down to the areolae of the breasts where they were present in large numbers. A few were seen over the sternum and many were present on the pubes, extending to the labia majora and in a triangle upwards to the umbilicus. Biopsy showed changes resembling those of chronic eczema, with round-celled infiltration most pronounced about the follicles. Though the apocrine glands themselves were not inflamed, the distribution of the papules supports the view that the disease represents a functional disorder of these glands associated with inflammation about the follicles into which they open. The disorder of function is believed to be due to some endocrine disturbance, and in fact stilboestrol gave considerable relief.

Malignant tumours

Derived from vessels

Kaposi's pigmentary sarcoma—E. E. Aegerter and A. R. Peale, who report four cases, describe Kaposi's sarcoma (idiopathic multiple haemorrhagic or pigment sarcoma) as a disease of mainly geographical incidence, affecting chiefly people from central or south-eastern Europe. It is commonest between the ages of forty and seventy and is very rare in children. Males are affected twenty times more often than females, and outdoor labourers more often than other occupational groups. Any part of the body may be the primary seat of the disease, but the cutaneous type which Kaposi originally described is the most common. In the authors' cases the skin was primarily affected in three patients; in the fourth the disease was confined to the wall of the right auricle. The lesion usually appears as a reddened macular area on one of the limbs, generally the leg. By degrees the colour changes to dusky red, then becomes bluish and finally brown or black, a change explained by microscopic examination which shows, first, increase of cavernous vessels, then haemorrhage into the tumour and finally pigmentation, probably produced by disintegration of the blood. In the early stages the sections resemble those of a cavernous haemangioma, but as time passes the sinuses are seen to be surrounded by increasing numbers of fusiform cells resembling young fibrous tissue cells and forming avascular masses into which haemorrhage eventually takes place. The nature of these cells is debatable, but the authors believe that they are of endothelial origin and that the tumours should be classed as angiosarcomas. The lesion soon becomes raised, and in its early stages looks like a varicosity; as it progresses it infiltrates the subcutaneous tissue and lymphatic vessels, causing oedema or even elephantiasis of the limb. At a later stage metastases usually appear in the viscera; glandular metastasis, although not common, may also occur. The disease as a rule is steadily progressive, although remissions may occur during which it remains stationary for lengthy periods. In the published cases the duration varied from eight months to twenty-five years, but is usually from five to ten years. A few cases are said to have regressed spontaneously. X-ray treatment probably gives the best results; the early lesions respond well, but they almost always recur and are then more resistant. Temporary good results have been claimed from treatment by arsenates given orally or by injection. The only one of the authors' patients who survived (it is not stated for how long) underwent amputation of the foot for eradication of multiple nodules.

Treatment

X-ray treatment.—In a paper read before the British Association of Dermatology and Syphilology B. W. Windeyer surveys the subject of X-ray treatment of malignant disease of the skin. The common types, namely basal-celled and squamous-celled carcinoma, can be treated either by X-rays or by radium. Of recent years the latter has largely supplanted the former, for the following reasons: (1) inconvenience of the apparatus and its inconstant output; (2) inaccuracy of methods of measuring dosage; (3) inadequacy of technique. The author points out that great improvements have been made in all these respects of recent years and he claims that X-ray treatment can give results equal to those obtainable by the use of

radium. It is essential that whatever form of radiation is employed the total duration of treatment should not be too long. Repeated small doses spread over weeks or months may be followed by the development of radio-resistance in the growth. At the Middlesex Hospital two types of apparatus are in use, one of 95 kilovolts and one of 200 kilovolts, the former for superficial growths, the latter for the more infiltrating types. Between 1938 and the end of 1941, 165 cases of basal-celled carcinoma and thirty-five cases of squamous-celled carcinoma have been treated. Small superficial lesions receive a single dose of 2500 r to 3000 r. For the more extensive and infiltrating growths the dose is 3000 r to 4200 r, divided into from six to nine daily applications. The single dose treatment, occupying only from ten to eighteen minutes, is very convenient but requires careful attention to make sure that the patient does not shift his position during the application. Of the whole series, 162 of the rodent ulcer cases resulted apparently in a cure. Twenty-seven of the patients with squamous-celled carcinoma were apparently cured, and in three others the lesion healed but glandular metastases developed.

Innocent infective conditions

Sarcoidosis

Clinical picture.—Carmen C. Thomas describes a series of fifteen cases of sarcoidosis observed for periods of from one to seven years. Three patients were white, twelve negroes; all but two were women. The age of onset varied from fifteen to forty-nine and in half the number of patients it was under thirty. Sarcoidosis is characterized by widespread infiltration of all the structures composing the reticulo-endothelial system. The course is usually slowly progressive and rarely leads to death. The disease, which is much commoner in negroes than in whites, is believed to be due to the tubercle bacillus, at least in the majority of cases. It may represent an immunity reaction. Monocytosis is common, it was found in over half of the present series of patients. Various types of cutaneous lesion are observed, including the miliary lupoid, the Besnier-Boeck sarcoid, the subcutaneous sarcoid and a psoriasiform papular variety recently described in American negroes. No treatment is known.

Aegerter, E. F., and Peale, A. R. (1942) *Arch. Path.*, **34**, 413.

Roxburgh, A. C. (1943) *Brit. J. Derm.*, **55**, 121.

Rulison, R. H. (1942) *Arch. Derm. Syph., N. Y.*, **46**, 66.

Thomas, Carmen C. (1943) *Arch. Derm. Syph., N. Y.*, **47**, 58.

Windeyer, B. W. (1943) *Brit. J. Derm.*, **55**, 113.

SKIN DISEASES: GENERAL

Aetiology

Metabolic causes

Fat metabolism—Preliminary observations on fat metabolism in certain skin diseases (psoriasis, eczema, seborrhoeic dermatitis and lichen planus) are reported by E. C. Dodds, H. MacCormac and J. D. Robertson. The experiments were made to test the theory that a humoral cause underlies many skin diseases, particularly psoriasis, in which Grutz and Berger claimed to have demonstrated a disturbance of fat metabolism. The authors' conclusions are that patients do not get any better on a low fat diet, or any worse on a high fat diet. The cholesterol content of the blood was estimated when the patient was fasting and at four, eight and twenty-four hours after the ingestion of 5 grammes (75 grains) of cholesterol. The only case which showed any abnormality was also the only case in the series of lichen planus in which the fasting blood-cholesterol was much raised, and the values obtained after cholesterol ingestion showed an extremely high rise and a delayed return to the fasting figure.

Clinical picture

Dermatitis atrophicans maculosa

Clinical course.—J. H. T. Davies and J. F. Smith describe two cases of a skin condition of which they could not find any other instance in the literature. The disease is difficult to classify but appears to belong to the somewhat ill defined group known as dermatitis atrophicans maculosa. (1) A labourer, aged thirty-two, complained of an itching skin disease of two years' duration, causing insomnia and consequent depression. Examination disclosed about twenty patches in various stages of evolution, varying from two to ten centimetres in diameter. They were situated at the posterior edge of the scalp, about the shoulders, on the extensor aspect of the forearms, in the lumbar region, on the lower abdomen and on the inner sides of the thighs. The initial lesion was in the suprapubic area among the hair and was represented by a smooth bald patch of slightly atrophic and wrinkled skin. A recent patch had a weeping eczematoid appearance, with infiltration and minute oozing points. Lesions of intermediate age resembled lichenified dermatitis with adherent non-silvery scaling. Each patch was surrounded by a zone of complete depilation with a sharply defined outer edge. Many types of treatment were tried without success. The disease gradually spread and the mental depression increased; when last heard of about five years after the onset, the patient was in a mental institution. (2) A lad of eighteen complained of a slightly itching eruption of about three years' duration. Patches similar to those seen in the first patient were found on the chin, neck, buttock, shoulder and arm. Hair loss on the patches was not complete and a hairless surrounding zone was observed only on the chin and neck. Treatment was without effect. In both patients the Wassermann reaction was negative and the blood count was normal. The

chief features shown by histological examination were hyperkeratosis, hypertrophy and oedema of the rete mucosum and papillae and replacement of collagen by fat.

Davies, J. H. T., and Smith, J. F. (1943) *Brit. J. Derm.*, **55**, 39.

Dodds, E. C., MacCormac,¹H., and Robertson, J. D. (1942) *Brit. J. Derm.*, **54**, 212.

SMALI POX

See also B.E.M.P., Vol. XI, p. 269; and Cumulative Supplement, Key No. 1416.

Incidence and epidemiology

Incidence

Outbreak in Glasgow.—C. K. Millard discusses the outbreak of smallpox in Glasgow in the summer of 1942. He emphasizes the following points (1) An initial mistake was made in diagnosing the first case, on board a ship from Bombay, as measles. The true diagnosis of confluent smallpox was not made until the ship reached Glasgow five days after the rash appeared (2) The great majority of the ship's crew of over 200 had recently been vaccinated and none developed smallpox. Of the minority, thirty-seven in number, seven contracted the disease and one died. One passenger aged twenty-three who contracted smallpox had been vaccinated three times, but not since the age of fourteen. A boarding medical officer who had not been vaccinated since infancy caught the disease. The importance of recent vaccination for anyone proceeding to or from the East needs no emphasis (3) No secondary case resulted from any of the ten 'ship' cases, a testimony to the efficacy of the precautionary measures taken. The 'city' group comprised twenty-one primary and four secondary cases. Of the former all but three occurred within ten days, suggesting a common source of infection, which, however, could never be traced. The occurrence of these cases soon after the arrival of the ship points to some connexion with the 'ship' cases; possibly with a missed case of the disease. Of the twenty-five 'city' cases eight patients had never been vaccinated, and these were the most severely affected, the rest had been vaccinated once, twice, or, in one instance, three times. The last patient had not, however, been vaccinated for twenty-two years. The mass vaccination campaign which was instituted was in the author's opinion an unnecessary measure. Such a procedure entails much expense and inconvenience and examination of the relevant dates shows that the outbreak was already practically over when mass vaccination was started. In the Leicester outbreak in 1903 the author, then Medical Officer of Health, adopted the policy of visiting every infected household and vaccinating contacts. Mass vaccination was not practised. Business went on, the life of the town was not interfered with and the epidemic was checked.

Clinical picture

Clinical types

Asiatic smallpox—P. B. Wilkinson, with experience as medical officer in the Colonial service at Hong Kong, especially of the most severe epidemic of 810 cases which occurred there in 1937–8 with a striking number of toxic cases, points out that this is one of the best examples of a diphasic disease. The major and minor (severe toxic and the ordinary) forms provide a remarkable contrast. The toxic form after twelve days' incubation gives rise to the sudden onset of rigors, fever, vomiting, headache and backache—the most outstanding features of the toxic form—which usually lasts three days. If the patient survives this period the temperature falls and focal lesions appear, in the gravest cases the temperature may be subnormal and death generally occurs before the sixth day and before the appearance of the focal lesions. Oral fetor is nauseating and unforgettable. Rapid enlargement of the liver may occur. The author does not believe that there is any treatment for the toxic form, but advocates painting the septic focal lesions daily with a saturated solution of potassium permanganate to relieve the patient's discomfort, and also the administration of sulphanilamide, as advised by Wilkinson in 1942.

Millard, C. K. (1943) *Brit. med. J.*, **1**, 288.

Wilkinson, P. B. (1942) *Lancet*, **2**, 67.

— (1943) *ibid.*, **1**, 120.

SPEECH DEFECTS

See also B.E.M.P., Vol. XI, p. 294.

Stuttering

Treatment

By extraction of teeth—C. E. Worth records the case of a boy who suffered from stammering and other nervous symptoms and who was cured by extraction of impacted teeth. The patient, aged eleven and one half years, stammered so badly that it was almost impossible to understand him and he had a nervous tic which was continuous and persisted even during sleep. At the time of his birth his mother was forty and his father fifty years of age. The condition developed when the boy was about four years old and it grew steadily worse. At the age of six he had an attack in which he fell down unconscious and remained so for from ten to fifteen minutes. He had been left-handed but at his first school had been taught to use his right hand. He had been at a school for stammerers but there had not been any improvement. The advice of a chiropractor was then sought and he recommended the parents to consult a dentist.

X-rays of the mouth revealed nine impacted teeth, namely the lower left bicuspid and all the second and third molars, both upper and lower. None of them were fully developed and they were all so interlocked that none could erupt. After the removal of enough teeth to provide room in the mouth, the patient's condition improved greatly and the nervous manifestations vanished.

Psychotherapy and re-education.—T. G. Leary regards stammering as a symptom of a fundamental disunity of the mind. The stammerer is convinced that he cannot speak; the condition is fundamentally a fear complex resulting from a succession of failures and progress is not possible until fear has been overcome. Stammer may be hereditary or may originate from shock, from maladjustment to environment, from imitation or from the forcing of a left-handed person to learn right-handed writing. Correction aims at readjustment of the personality to the environment. In some cases psychoanalysis is a necessary beginning; as a rule, however, the stammerer's inhibitions can be discovered by observation and questioning. Training in elocution and breathing are at most subsidiary means of treatment. The stammerer must first be induced to relax and when he begins to speak to do so rhythmically as though he were singing or reciting. The speaking exercises must be very simple at first. Class training is particularly valuable. The stammerer must be persuaded to use rhythmic speech on all occasions, not only during periods of treatment. As he progresses more advanced exercises (asking and answering questions; reading aloud) are given, and finally he may take part in class debates and in discussions. It must be impressed upon the pupil that rhythmic speech is agreeable to the hearers provided that the voice is pitched low.

With review of aetiology.—S. Cobb, Bullard Professor of Neuropathology, Harvard Medical School, points out that in order to understand speech defects some knowledge of the development of speech in man is necessary. In phylogeny there is clearly a close relationship between the development of binocular vision, manual skill and finally a leading hand and leading cerebral hemisphere. When man's shrew-like ancestors took to trees and left behind them quadrupedal locomotion, their fore-limbs were emancipated to become hands, and the possibility of dexterity developed. Other vertebra specialize and reach narrow superiority by unique development of one type of sense organ. Man excels because of lack of specialization. His speciality is a leading cerebral hemisphere, and its even development allows for the association between the various sensory impressions, their receiving stations, and mechanisms that have made intellectual behaviour. The dominance of the left cerebral hemisphere is, as regards speech, pronounced in the right-handed individuals who make up 75 per cent of the population, but speech functions are not confined to the left hemisphere. In the central nervous system of man speech functions are integrated at five levels which are not exact and which to some extent overlap. Consideration of the common lesions, the clinical results of the lesions and the treatments are tabulated. The level 1, the neuromuscular, contains the obvious developmental defects such as hare-lip and cleft palate. At level 2 the corticobulbar neurones are often involved in syphilis, and by softening due to arteriosclerosis, tumours and encephalitis epidemica. The level 3 is concerned with cerebral coordination, and may suffer in multiple sclerosis and paralysis agitans. Level 4 is divided into (a) factors concerned with symbolism (words), apraxia, motor aphasia, agraphia, amusia, and (b) lateral dominance—clinically, stammering, slow reading, ambidexterity. Level 5 is the most highly integrated and least localizable, it is associated with the great association of the frontal and parietal lobes, and brings in memories, individual life experiences and the impact of one person upon another. When the personality of the subject of a speech defect is clearly known and what is left of the speech mechanism realized, the treatment can be outlined. If aphasia is complete, there is little to be done except to stimulate the patient to more activity and more contact with environment by moving about, by occupational therapy and by re-education of the nervous system. Orton's method of treatment, aimed at making the patient fix his lead in a chosen hemisphere, is an advance in treatment. But it must not be assumed that every ambidextrous child will have difficulty in symbolism, perhaps 10 per cent of the population are somewhat ambidextrous and only about 1 per cent have difficulty. From the standpoint of treatment a left-handed child should not be forced to be right-handed in any way. Stammering is a psycho-neurosis, and experience in the treatment of stammerers has shown that working on the neurosis without any attention to the speech will sometimes cure the stammering. Probably the best methods are those that combine psychotherapy, socialization and speech exercise. Most stammerers probably inherit an inferior speech apparatus, often linked with a left-handed or ambidextrous tendency.

Cobb, S. (1943) *Bull. N Y. Acad. Med.*, **19**, 34.

Leary, T. G. (1942) *Med. J. Aust.*, **2**, 119.

Worth, C. E. (1942) *J. Amer. dent. Ass.*, **29**, 1546.

SPINAL CORD DISEASES

See also B.E.M.P., Vol. XI, p. 302.

Tumours

Extrathecral tumours

Spinal lymphoblastoma.—G. S. Baker reports two cases in men, aged forty-nine and forty-one years respectively, as examples of spinal lymphoblastoma, including under this broad category

lymphosarcoma (large-celled and small-celled, follicular and reticulum cell forms), leukaemia and Hodgkin's disease. The disease is clinically remarkable as being prone to imitate other organic syndromes such as haematuria and pancreatic calculus. Of the two reported cases one patient was cured by complete removal of the tumour. At the Mayo Clinic twenty-two patients with spinal lymphoblastomas have been treated by surgical removal of the tumour.

Baker, G. S. (1942) *Proc. Mayo Clin.*, **17**, 588.

SPRUE, TROPICAL

See also B.E.M.P., Vol. XI, p. 419; and Cumulative Supplement, Key No. 1453.

Morbid anatomy and pathology

Biochemical considerations

Causes and treatment of steatorrhoea—H. S. Stannus deprecates any attempt to classify, before their true pathogeny is known, the diseases which are characterized by steatorrhoea. Suggested causes are (1) chronic jejuno-ileal insufficiency with consequent defects of secretion and absorption, (2) paralysis of the muscularis mucosae with loss of the pumping action of the villi; (3) damage to the intramural nervous system, (4) blocking of the lymphatic vessels. Adequate supporting evidence cannot be found for any of the above theories. Stannus believes that the radiological changes—loss of mucosal pattern in the jejunum, disappearance of valvulae conniventes and so on—are secondary, and that they demonstrate the reaction of the bowel to its abnormal and bulky contents. Estimations of the amount of fat in the stools are reduced in value by the fact that the normal figure is undetermined, and account is not always taken of the amount of fat which is ingested. The theory is postulated that sprue results from failure of absorption of the fatty acids and cholesterol derived from the splitting of fats. The unsplit neutral fats are absorbed normally, except in so far as the mechanical effect of the mass of fatty acid in the bowel may interfere with emulsification. The above hypothesis is based on the 'partition' theory of fat absorption, which maintains that the routes of absorption for split and unsplit fats are different, being respectively the portal venous system and the thoracic duct. Phosphorylation is an essential step in the process of digestion of the split fats, and it is suggested that this is the stage at which failure occurs in sprue. A similar failure of phosphorylation may be responsible for the primary loss of power to absorb glucose, resulting in the low flat blood sugar tolerance curve characteristic of sprue. Failure of phosphorylation probably results from deficiency of some enzyme, and the enzyme in question may contain as an integral component vitamin B₆ (pyridoxin). Deficiency of this vitamin would account for the recognized beneficial effects of the administration of liver extract in sprue which should be reckoned among the diseases which are due to malnutrition. Variations in the fatty acid composition of the diets in different countries may explain the geographical distribution of the disease: American butter, for instance, differs considerably in composition from English butter.

Differential diagnosis

From pernicious anaemia

The neutral red excretion test—A. R. Olleros discusses the differential diagnosis of tropical sprue and pernicious anaemia, which are sometimes indistinguishable by ordinary methods. In a group of twenty-five patients with sprue, two showed histamine-resistant achlorhydria. In all but two, bacteria were isolated from the stomach contents, in one the bacteria were all Gram positive, in eight they were Gram negative and in fourteen they were of both types. Invasion of the stomach by Gram negative flora from the large intestine occurs also in pernicious anaemia; its occurrence in sprue, in which free hydrochloric acid is present in the majority of cases, indicates that achlorhydria is not responsible. The suggestion is made that it results from a deficiency of sulphocyanate in the saliva, which deficiency has been demonstrated in patients with pernicious anaemia, but no evidence is offered to support such a view. Gastroscopic examination was performed in three groups of patients with sprue. In cases which showed the complete syndrome, signs of atrophic gastritis were observed but they were less pronounced than in most cases of pernicious anaemia, in patients who showed an incomplete syndrome the signs were still less obvious, and, in patients with latent sprue who had been treated by liver extract, atrophic gastritis rarely persisted. The neutral red excretion test was performed on forty-nine patients in the following manner. After a fast of twelve hours a fractional examination of the gastric secretion was made, and then 5 cubic centimetres of 1 per cent solution of neutral red was injected intramuscularly; samples of gastric juice were withdrawn every five minutes until the dye appeared. All the patients were found to eliminate neutral red through the gastric mucosa, even when a degree of atrophy leading to histamine-resistant achlorhydria was present. The test offers a means of differentiating tropical sprue from pernicious anaemia in which condition the gastric mucosa shows a much higher grade of atrophy and is incapable of excreting neutral red.

Olleros, A. R. (1942) *Amer. J. digest. Dis.*, **9**, 261.

Stannus, H. S. (1942) *Trans. R. Soc. trop. Med. Hyg.*, **36**, 123.

STERILITY

See also B.E.M.P., Vol. XI, p. 447; and Cumulative Supplement, Key Nos. 1455–1457.

General aspects

Causes of infertile marriage

Investigation and treatment.—J. W. Bourland, Sen. discusses, from the gynaecologist's standpoint, the problem of the sterile couple. The first step is to assess the relative responsibility of husband and wife, and here close cooperation with the urologist is essential. The following routine procedure is advised; a detailed history is obtained and an examination which includes Wassermann test, complete blood count and determination of basal metabolism, is made of both partners. Unsuspected anaemia may be discovered, and the metabolic rate is an indication whether or not thyroid extract should be given. Examination of the semen is carried out next to determine the total quantity of ejaculate, the number of spermatozoa per cubic centimetre, their motility, the percentage of abnormal forms and the number of hours that motility is retained when the semen is incubated at 37 °C. Unless the male is found to be hopelessly sterile, further examination of the female is carried out. The viscosity of the cervical secretion is estimated by means of the Hühner test; if the viscosity is high, better drainage can be secured by diathermy or electrocautery applied to the cervix. The patency of the tubes is tested by carbon dioxide injection; if the pressure rises to 200 millimetres an injection of iodized oil is given immediately, an absorbable compound (Iodochlorol) being used in order to avoid the possible ill effects of iodized oil. If the uterine tubes are blocked at the fimbrial ends, repeated inflation may open them. Endometrial biopsy may be helpful. Treatment in both partners includes correction of any abnormalities, either local or general, that may have been discovered, and advice should be given regarding the fertile period of the month.

Sterility in the female

Investigation of patients

Electrical determination of ovulation. A method which is believed to make possible the determination of the time of ovulation is described by L. Langman and H. S. Burr. A recording apparatus was used to measure the electrical variations which were produced by uterine movements in each phase of the menstrual cycle during fourteen cycles in nine women. The studies showed that most commonly (in nine of the fourteen patients) the cervix was positive throughout the menstrual cycle to the indifferent electrode (ankle) by 5 to 25 millivolts, increasing to 30 or 35 millivolts four or five days before the onset of the menstrual flow; in nine of the fourteen patients on certain days, at least one in each cycle, the cervix became negative by an equivalent amount. In one woman artificial insemination with donor's sperm was carried out on the second of two successive 'negative' days and resulted in conception. The woman's husband had azo-spermia and mating had previously been infertile. In a second case artificial insemination had been carried out ten times without success, but when it was practised on a 'negative' day, it was followed by pregnancy. The success of artificial insemination in the two foregoing cases suggests that ovulation occurred during the negative period. The negative readings were obtained at various times during the cycle, even, in one case, during menstruation.

Recent advances. I. C. Rubin discusses the present state of the diagnosis of female sterility. Thirty years ago the female was usually the only partner of a sterile marriage to be specially examined, and examination was not very thorough, it is not surprising that the prognosis was as often wrong as right. During the last twenty years considerable progress has been made on the lines stated below. (1) It is recognized that the male partner may be, and often is, responsible for the failure to conceive, this was largely due to the work of M. Hühner (1924) whose test has become more or less the special task of the gynaecologist, with some provisos, if it shows an ample number of motile spermatozoa with good morphological characteristics, it almost exonerates the male partner. (2) The second step was the determination, by a clinical test, of patency of the upper part of the female genital tract. (3) The third step was the recognition of the importance of the constitution of the married partners. (4) The fourth step was the further development of the knowledge of hormones. The causes of female sterility may be local, which are more often mechanical than functional, the latter being bound up with disturbances of the endocrine and nervous systems or due to some constitutional states. The mechanical causes are obstructive, due to anatomical displacements. According to S. W. Meaker, who analysed the data of seventy-five sterile marriages, constitutional factors play almost as important a part as do local genital causes. The constitutional factors include chronic infections of the tonsils and sinuses, syphilis, protein starvation, vitamin deficiency, alcoholism and diabetes mellitus. Lead poisoning, a constitutional factor, is occasionally found in the husband. Hypertension, in Rubin's experience, appears to exert more of a deleterious influence upon an existing pregnancy than upon the ability to conceive. Rubin discusses sterility from the endocrine standpoint; the gross disturbances are obvious, although rare. Of far greater clinical importance in relation to sterility are the less prominent or intermediary types, the *French formes frustes*. It is pointed out that in some quarters the investigation of sterility is overdone with tests which may react adversely on the woman's mental state.

Treatment

The safe and fertile periods.—B. Gilbert discusses the periodicity of menstruation in its practical bearings. He examines the evidence for a possible association between the menstrual rhythm and the lunar cycle, and concludes that such relation has not been established. The

average duration of the menstrual cycle appears to be twenty-nine \pm 0.19 days, but it is subject to individual variations within fairly wide limits. In 90 per cent of women the interval between successive periods ranges from twenty-five to thirty-six days. About 50 per cent of all women differ from their average by at least \pm two days, the remainder by \pm two days or less. The average interval decreases with advancing age by about one day for each five or six years. Marriage and parity do not affect the rhythm, nor is there any evidence that it is influenced by occupation. Variations in the cycle may be related to a varying harmonic output of the pituitary gland or of the ovarian follicular system, to mechanical resistance to ovulation or to variations in the rate of development of the follicle which is about to rupture. Maturation of more than one follicle may occur in each cycle. Fertility and sterility are necessarily associated with the menstrual cycle. Allowing for variations in the length of the cycle, in the average woman the ovulation time has been calculated to vary between the eleventh and the twenty-second days. Since spermatozoa may live for two days and since the ovum is believed to live for one day after ovulation, the total fertile period would be, on computation, fourteen days in each cycle. The fact that the fertile period is so long strongly suggests that multiple ovulation is more common than formerly has been believed. It is clear, therefore, that the so-called safe period is unreliable.

Sterility in the male

Conditions affecting fertility

Testicular biopsy in diagnosis —R. S. Hotchkiss pleads for the value of testicular biopsy in the diagnosis of complete absence of spermatozoa from the semen, which means absolute sterility in the male; this procedure facilitates adoption of the correct treatment. The causes of this defect may be either (1) mechanical obstruction of the efferent ducts, or (2) aspermatogenesis. The obstructive form may be associated with thickening of the epididymes, whereas atrophied testes point to insufficiency of the germinal epithelium. External examination of the genitals does not always settle the diagnosis, and a clear indication for operation can be afforded by the help of biopsies, the findings pointing to obstruction or to congenital anomaly of the efferent tract; thus if a testicular biopsy shows well differentiated germinal epithelium and if several seminal ejaculations are devoid of spermatozoa, operation is then called for. The procedure of obtaining testicular material does not demand any special skill and does not entail much discomfort. The genital organs are prepared for operation and a small area of the scrotal skin is anaesthetized by 1 per cent novocain (procaine hydrochloride). An excision is made down through the tunica vaginalis and a V-shaped piece of testis is removed; the procedure is then repeated on the other side, and the pieces are fixed in Bouin's solution. The seminiferous tubules may contain normal or defective epithelium, the epithelium may be arrested at an early stage of development, its place may be taken by hyaline material or the tubules may be surrounded by profusely proliferating fibrous tissue. Faulty spermatogenesis may probably be ascribed to (1) an inherited gametogenic factor, a theoretical possibility, (2) a deficiency of vitamins, (3) endocrine disorder and (4) constitutional disorders.

Bourland, J. W. Sen (1942) *Urol. cutan. Rev.*, **46**, 502

Gilbert, B. (1942) *S. Afr. med. J.*, **16**, 355

Hotchkiss, R. S. (1942) *Bull. N.Y. Acad. Med.*, **18**, 600.

Langman, I., and Burr, H. S. (1942) *Amer. J. Obstet. Gynec.*, **44**, 223.

Rubin, I. C. (1942) *Bull. N.Y. Acad. Med.*, **18**, 537

STOMACH, TUMOURS AND SOME OTHER CONDITIONS

See also B.E.M.P., Vol. XI, p. 476; and Cumulative Supplement, Key Nos. 1461-1464

Malignant tumours of the stomach

Macroscopically

Gastric polypi and polypoid gastritis —L. I. Spriggs and O. A. Marxer of Ruthin Castle give a comprehensive review of gastric polypi and of polypoid gastritis, based on their own observations, especially radiological, and on those of other workers. Among 4,424 persons examined radiologically during eighteen and a half years, so far as the alimentary canal was concerned ten examples of a gastric polypus and one of a duodenal polypus were recognized by the authors. Thirty-five communications on other cases of gastric polypi with a clinical history were made by colleagues of the above investigators, the clinical details being compared with those mentioned in fifty-four cases published by other authors; this allows a review to be made of the signs and symptoms in a hundred cases. Twenty-four specimens without a clinical history but in pathological museums are also tabulated. The term polyadenoma or polyposis is used when there are so many tumours, that they are not easily counted. Polypi may be single or multiple, stalked or sessile, and include papillomas, adenomas, leiomyomas, adenomyomas, neuromas, angiomas, lipomas, angio-endotheliomas and cysts; the main types of polypi fall into three main groups, namely (1) papilloma or adenoma, (2) leiomyoma and (3) polypoid hyperplasia ascribed to irritation. Apart from the polypi the gastric mucosa may be normal, or there may be inflammatory changes, atrophic gastritis, or carcinomatous changes, but the last named is less common in the stomach than in the colon and, if there are several gastric polypi, very seldom more than one shows carcinomatous change. Any part of the stomach may be the site of polypi, but the body and pre-pyloric area are most often affected. Just over half of the sixty-nine cases were of single lesions. Small polypi may not

cause any symptoms but this is unusual; dyspepsia is more common. The diagnosis is made by radiology and in suitable cases by gastroscopy. In cases of polypoid hyperplasia of the gastric mucosa with peptic ulceration, the gastric juice usually contains free hydrochloric acid. This monograph gives much information; thus among the 4,424 radiographical examinations there were 104 cases of malignant disease of the stomach and 570 cases of peptic ulcer. The authors have not seen the combination of pernicious anaemia with gastric polyp which has been reported occasionally.

Spriggs, E. J., and Marxer, O. A. (1943) *Quart. J. Med.*, N.S., 12, 1.

STRABISMUS

See also B.E.M.P., Vol. XI, p. 492; and Cumulative Supplement, Key No. 1465.

Comitant (concomitant) or non-paralytic squint

Treatment

Orthoptic technique - Julia E. Lancaster describes the orthoptic technique as applied to alternating squint. All orthoptic treatment is an educational process which is adapted to each individual. The first step is to find out what the patient can do. Anomalous correspondence may be detected by the after-image test or on the major amblyoscope, which measures the exact angle of anomaly and can be used for children down to three years of age. Correction of anomalous correspondence is carried out by means of the synoptophore, and requires from four to twenty-four or more half-hour sessions. When correction is complete the patient is ready to learn fusion. Of about 200 patients only one failed to obtain fusion with the synoptophore. Fusion having been established, the next step is to develop amplitude, that is to maintain fusion while the eyes move. At this stage surgery is sometimes helpful. The patient must be taught to overcome suppression, in spite of the diplopia which results. He is made to practise monocular fixation and subsequently binocular fixation. When once he has achieved true binocular perception without suppression and with some amplitude, he is ready to transfer his skill to casual seeing. This stage is another step in orthoptic training where progress may come to a standstill and surgery may be indicated, if the patient can fuse for casual seeing he can practise constantly until fusing becomes habitual and he is ready for bar-reading, if he is old enough to read. It is very difficult to perfect non-reading patients in binocular habits. Ability to bar-read completes the cure.

Operative results - J. H. Dunnington and M. C. Wheeler present their operative results in 211 cases of convergent strabismus. The criterion used, although admittedly not always agreeing with that of the patient or of his parents, was the degree of deviation which remained. The patients were classed according to age in three groups: three years old or under, three to eight years; and over eight. In 14.7 per cent the operation was a failure, that is either the original deviation was reduced by less than 50 per cent, or overcorrection exceeded ten prism dioptres. Reasons could not be found for the failures. Some patients required more than one operation. Undercorrection (under 10) resulted in 44 per cent, overcorrection (over 10) in 13 per cent, and in 43 per cent the eyes were straight. The highest proportion of overcorrections occurred in the age group of three to eight years. Better results were obtained in monocular than in alternating strabismus.

Dunnington, J. H., and Wheeler, M. C. (1942) *Arch. Ophthalm.*, N.Y., 28, 1.

Lancaster, Julia E. (1942) *Amer. J. Ophthalm.*, 25, 866.

SYMPATHETIC AND PARASYMPATHETIC NERVOUS SYSTEM

See also B.E.M.P., Vol. XI, p. 503.

Tumours of the autonomic system

Tumours of sympathetic nerves

Symphatogonioma of the anterior superior mediastinum - S. Sailer records the case of a negro, aged sixty-five, admitted to hospital in a drowsy and stuporous state and who died two days after admission. Necropsy showed that there had been acute influenzal cerebrospinal meningitis as well as broncho-pneumonia of the left lower lobe. A symphatogonioma of the anterior superior mediastinum, measuring 5 centimetres in diameter, was found; it was firm and round, overlying the superior vena cava and attached to it by adhesions. The tumour arose beneath the pericardium, probably from within the sympathetic rami of the deep cardiac plexus. There were evidences of chronic obliterative pericarditis with myocardial hypertrophy and dilatation, chronic emphysema and pleuritic adhesions and a chromophobe adenoma of the anterior part of the pituitary gland. The author points out that tumours arising in the sympathetic, of all kinds, are widely spread throughout the body; they are rather frequent in the adrenal medulla and have also been reported in the abdominal, cervical, thoracic (of which thirteen cases are here tabulated) and pelvic sympathetic nerves, the jejunum, the coeliac ganglion, the mesentery, the coccygeal body, liver, uterus, nasal cavity and skin. The tumour was strikingly encapsulated, for only in one place did a microscopical field show infiltration of the surrounding tissues by tumour cells. In most cases metastases are widespread and early.

Sailer, S. (1943) *Amer. J. Path.*, 19, 101.

SYPHILIS

See also B.E.M.P., Vol. XI, p. 526; and Cumulative Supplement, Key No. 1467.

Aetiology

Infectivity of early and late lesions

In prostitutes.—F. Pinkus has attempted to answer two questions: (1) How long does syphilis remain infectious? and (2) How should one explain the exceptionally late occurrence of infectious lesions? He has analysed a group of 2,856 Berlin prostitutes who had been infected more than ten years previously. Contagious lesions were found in 116 (4 per cent) of the patients more than seven years, and in fifty-eight (2 per cent) from ten to twenty-seven years, after infection. The appearance of such lesions might be due to relapse, rejuvenation—a term used for recurrence of all the stages of the disease—and reinfection. The author is not convinced that rejuvenation ever does occur and he considers that the third explanation is probably the true one and that, in prostitutes particularly, repeated infection can and does take place. The incidence of syphilis in prostitutes is high; the Berlin police figures show that it is present in more than 50 per cent. Many women continue to ply their trade up to an advanced age, and the author's analysis shows that many old prostitutes are just as capable of transmitting syphilis as are young ones who have been infected recently.

Congenital syphilis

Clinical picture

The teeth.—B. G. Sarnat and N. G. Shaw describe their observations on the dental manifestations of congenital syphilis, and review the literature. Of a group of seventy-three congenital syphilitic children twenty-two (30 per cent) showed characteristic dental changes. The effects of syphilis on the deciduous and on the permanent teeth are different. The deciduous teeth show disturbances of enamel development; four children who still had their deciduous teeth showed hypoplasia of the enamel. The teeth were badly worn and carious. Alteration of shape was not apparent. The characteristic effect of syphilis upon the permanent teeth is a disturbance of the dentino-enamel junction with consequent dwarfing of the crown. Of the children whose permanent teeth were already erupted, twenty-two had Hutchinsonian upper central incisors. In fourteen, in addition to the convergence of the two lateral margins towards the cutting edge, a mid-incisal notch was present, varying in character from shallow to deep. In some cases the lower incisors showed similar changes. Examination of the unerupted teeth by X-rays revealed characteristic Hutchinsonian incisors in every instance in which the deciduous teeth showed enamel aplasia. The first molars were affected in some cases although not as constantly as were the central incisors. On radiological examination of the affected teeth, pronounced convergence in the mesiodistal diameter of the dentino-enamel junction was observed. The authors point out that the clinical course of the disease cannot always be correlated with the dental changes. Several of the children had a history of severe syphilis but there were not any characteristic changes in the teeth, while in others the history was comparatively uneventful but dental changes were pronounced. The Hutchinsonian incisor and the bud or mulberry molar are not a reliable index of the severity of the disease during infancy. These developmental disturbances of the teeth have been found only in congenital syphilis.

Treatment

The use of the described remedies and other measures for the prevention and treatment of syphilis

Prevention and treatment of congenital syphilis—H. H. Perlman, writing from the Sigma Clinic at Philadelphia, points out that the classical picture of congenital syphilis is very rarely seen nowadays. Thanks largely to the campaign which has been carried on by the surgeon-general of the United States Public Health Service, the incidence of congenital syphilis has been reduced greatly in recent years. To an increasing extent syphilitic mothers are diagnosed and are treated before delivery, and syphilitic offspring are treated before the signs of the disease become manifest. Stress is laid on the importance of gaining the confidence and cooperation of older children, of accurate diagnosis and of adequate but not excessive treatment. At the Sigma Clinic the treatment of early cases is usually continued without an interval for a year and, according to the serological observations which are made during that period, it is then either continued, is discontinued or is modified. If both Wassermann and Kahn tests have become and remain negative, treatment is stopped, but tests are made at intervals for another year. The patient, if free from serological and physical signs of active disease, is then required to report for examination twice at intervals of six months, and thereafter once a year, until puberty is reached. The spinal fluid is tested at least once during the course of treatment and, in the case of infants under one year, the long bones are X-rayed. If the Wassermann reaction remains positive but active lesions are not evident, specific treatment is discontinued after three years. In late cases 'rest periods' are allowed during treatment. Neosarsphenamine or sulpharsphenamine and bismuth salicylate, given in rotation, are the remedies usually employed at the Sigma Clinic.

Perlman, H. H. (1942) *Urol. cutan. Rev.*, **46**, 424.

Pinkus, F. (1942) *Urol. cutan. Rev.*, **46**, 442.

Sarnat, B. G., and Shaw, N. G. (1942) *Amer. J. Dis. Child.*, **64**, 771.

TETANUS

See also B.E.M.P., Vol. XII, p. 1; and Cumulative Supplement, Key No. 1481.

Aetiology

Trauma

Tetanus after an eye injury.—Tetanus after an eye injury is so uncommon that J. O. Wetzel, who reports a case, has been able to collect only thirty other cases from the literature. His patient, a farmer aged thirty-nine, was admitted to hospital suffering from a perforating wound of the left eye-ball with prolapse of the iris and escape of the vitreous humour, caused by a nail which he had been driving and which had ricocheted into his eye. The man was given a prophylactic injection of 1,500 units of tetanus antitoxin. The wound in the eye was repaired after excision of the prolapsed iris, and the patient left hospital on the eighth day. Four days later signs of tetanus developed and he was readmitted. Intensive antitoxin therapy was begun after subcutaneous desensitization, a total of 375,000 units being given by intrathecal, intravenous and intramuscular injections. The injured eye was removed two weeks later, as soon as convalescence was established. The patient eventually made a good recovery.

Immunity and immunization

Natural and acquired immunity

Studies in children.—Active and passive immunity to tetanus has been studied by Jean V. Cooke and F. G. Jones in thirty-four children. Four of these had suffered from tetanus and had recovered. The remaining thirty were in good health and were experimentally immunized either passively with tetanus antitoxin or actively with tetanus toxoid. The antitoxin titre of the blood was estimated at intervals afterwards and the duration of immunity was thus determined. Passive immunity conferred by small doses (1,500 units or less) of antitoxin was found to last for only about three weeks. Larger doses produced correspondingly prolonged immunity. With doses of 100,000 units or more the blood serum still showed 0.01 unit per cubic centimetre after from eight to eleven weeks. It was confirmed that toxoid produces active immunity only when the subject has had a 'sensitizing' dose, and is inhibited by excess of foreign antitoxin in the blood. Thus active immunization with toxoid is successful only when passive immunity has reached a comparatively low titre. Attempts to hasten the development of active immunity by repeated injections of toxoid on alternate days had no result. No immunity developed in the children who recovered from tetanus and who had all received large quantities of antitoxic serum.

Cooke, Jean V., and Jones, F. G. (1943) *J. Amer. med. Ass.*, **121**, 1201.

Wetzel, J. O. (1942) *Amcr. J. Ophthalm.*, **25**, 933.

THYMUS GLAND DISEASES

See also B.E.M.P., Vol. XII, p. 23, and Cumulative Supplement, Key No. 1483.

Diseases of the thymus gland

Tumours

Lympho-epithelioma.—F. P. Weber and K. Blum record the case of a woman, about fifty-nine years of age at the time of her death. At various times she had complained of a severe form of acroparesthesia and numbness (no real anaesthesia) of the right lower limb and afterwards of the right upper and both lower limbs. Radiologically there was a rounded mass continuous with and moving with the heart shadow. Necropsy showed a multilocular cystic mass about the size of a large orange and weighing 112 grammes, the multilocular cystic central part had a honeycombed appearance. Most of the cysts communicated with each other and contained a slimy, translucent mucoid fluid which macroscopically suggested pus, but microscopically showed cellular material—tissue mast cells, which were not clearly differentiated from cells stained in other ways. The mass was a true lympho-epithelioma undergoing aseptic necrotic involution. There were not any metastases nor any microscopic evidence of malignant change. Thymic lympho-epitheliomas seem in some instances to exert an endocrine effect, and to be specially prone to cause myasthenia, as pointed out by C. Weigert (1901) when he erroneously regarded the 'lymphorrhages' in muscles as secondary growths. The mediastinal mass did not contain normal Hassall's corpuscles. The thyroid was slightly enlarged from adenomatous activity. A photomicrograph shows the characteristic epithelioid and lymphocyte-like cells.

Status thymico-lymphaticus

Thymic death

Aortic diameter in status lymphaticus.—W. G. Millar and T. F. Ross analyse the findings as regards the circumference of the aortic orifice in connexion with status thymico-lymphaticus and the liability to accidental death, as shown by 300 necropsies at the Royal Infirmary, Edinburgh. The necropsies were generally consecutive, but cases of advanced dilatation of the atheromatous aorta were excluded. Thymic gland enlargement as an essential sign of status lymphaticus has been disputed, and the most constant other sign appears to be narrowing of the aortic orifice, which is easily measured; the authors laid the aorta open flat, and measured it by a scale at the level of the fourth intercostal artery. Of the 300 necropsies, twenty-six cases were the result of accident, and the mean value of the aortic measurement in the accident cases was 1.48 millimetre less than that in the non-accident cases. The mean size of the aorta in patients dying as a result of accident is significantly smaller than in those

dying from disease. The difference between the two vessels is not due to dilatation of the aorta but to developmental hypoplasia of the arterial system in the fatal accident series. This hypoplasia is connected, probably indirectly, with liability to accident, and is the most reliable guide to the existence of status lymphaticus. The latter should be regarded as a real condition and should regain, at all events, some of the importance formerly attached to it as a factor in sudden and unexpected death.

Millar, W. G., and Ross, T. F. (1942) *J. Path. Bact.*, **54**, 455.

Weber, F. P., and Blum, K. (1942) *J. Neurol. Psychiat.*, **5**, 148.

Weigert, C. (1901) *Neurol. Zbl.*, **20**, 597.

TORULOSIS

See also B.E.M.P., Vol. XII, p. 52

Clinical picture and course

Cerebrospinal torulosis

Torulosis of the central nervous system—D. Blair records a case of torulosis of the central nervous system. This rare disease, for which no specific treatment is known, results from infection by a yeast-like organism. The mode by which it gains access to the body has not been determined. A man, aged forty-five, was transferred to a mental unit for observation, he was restless and required restraint, and he was mentally confused and hallucinated for all senses. The history showed that his illness had begun twelve weeks previously with severe headache, increasing pyrexia and malaise. He was admitted to hospital, where slight neck rigidity was noted. The symptoms gradually abated and he was discharged after five weeks. The headache, however, returned, and he was readmitted twelve days later, when Kernig's sign and Brudzinski's signs were positive, the tendon reflexes were increased and the left pupil was irregular. The patient gradually went downhill and mental symptoms developed, on account of which he was admitted to the mental unit. He became more and more restless and confused until, five days after admission, he suddenly became comatose and died. Torulae were isolated from the cerebrospinal fluid during life. Necropsy showed the typical picture of torulosis of the central nervous system and elsewhere. The blood vessels of the meninges and brain were congested and the surrounding tissues were injected. The ventricles and the sub-arachnoid space over each hemisphere were filled with the yellow brown gelatinous material characteristic of the infection. No other macroscopic evidence of torulosis was observed. The lungs showed typical pinkish patches of consolidation dotted with minute yellowish spots. Small colonies were present also in the kidneys.

Blair, D. (1943) *J. ment. Sci.*, **89**, 42.

TOXICOLOGY: HOMICIDAL, SUICIDAL AND ACCIDENTAL POISONING

See also B.E.M.P., Vol. XII, p. 59, and Cumulative Supplement, Key Nos. 1491–1527.

Synthetic organic substances

Hydrocyanic acid

Potassium thiocyanate in hypertension.—W. O. Russell and W. C. Stahl have collected from the literature five fatal cases of poisoning by potassium thiocyanate given for hypertension, and add one of their own. They emphasize the necessity for caution in using the drug, which appears to be growing in popularity, the margin between the effective and the fatal dose seems in some patients to be a very narrow one. In the case here recorded, in a man aged fifty-two, the blood pressure was 234/140 millimetres Hg, there was albuminuria and the renal function was poor. The patient received 6 grains (0.4 grammes) of potassium thiocyanate per day and after ten days the blood pressure had fallen to 160/100, the blood cyanate concentration was 15.2 milligrams per cent. Administration of the drug was continued for another week, when the patient became weak, mentally confused and progressively more drowsy. On the fourth day the blood cyanate level was 21.7 milligrams, the non-protein nitrogen rose steadily to 72 milligrams on the twelfth day, when the patient became comatose and died. Necropsy did not show any changes that could be specifically attributed to cyanate poisoning.

Sulphonamides

Fatal toxic effects of sulphathiazole.—M. A. Simon and M. Kaufmann record fatal sulphathiazole poisoning in a man, aged forty-four years, who two years before had tolerated the drug well; he was admitted to hospital for incision of an ischio-rectal abscess after having taken 60 grains (4 grammes) of sulphathiazole. After operation he took more than 180 grains (12 grammes) of sulphathiazole and in a few days suddenly developed a temperature of 105° F. and the drug was discontinued; but on the ninth post-operative day it was noted that oliguria and azotaemia were present. Two days later the patient showed an erythematous rash on the face and body, and death occurred on the fourteenth post-operative day. The necropsy showed extensive focal necroses of the liver, kidneys, spleen, heart, and adrenal glands, which were regarded as probably being due to the toxic action of sulphathiazole; it is concluded that these toxic lesions may occur even when the blood concentrations of sulphathiazole are within the so-called 'safe' range. The authors collect and review previously recorded cases, the first having been reported by A. L. Hoyne and G. W. Larrimore in 1941; two series of four reports each were published by M. Lederer and P. Rosenblatt and by W. C. Merkel and R. C. Crawford in 1942.

Inorganic and metallic

Mercury

Intravenous mercuria administration.—M. H. Barker, H. A. Lindberg and M. E. Thomas report the deaths of four patients as a result of intravenous administration of a mercurial diuretic, and describe the experimental induction of fatal ventricular fibrillation in dogs by the same means. All the patients had suffered from some chronic wasting disease and oedema had been present for several months; three of them had received numerous injections (from 15 to 200) before the fatal dose; the fourth died after the first injection. One patient had a severe reaction after a dose of 2 cubic centimetres of mercupurin, but recovered; three months later, because of a return of oedema, he was given the injection (2 cubic centimetres of salyrgan) from which he died. In three of the cases the drug was given quickly in a small amount of fluid. The sequence of events was much the same in each; within from two to five minutes gross cardiac irregularity developed, with cyanosis and dyspnoea, unconsciousness and death. The fourth patient was ordered to have 1 cubic centimetre of salyrgan in a saline drip transfusion, this had been running for thirty minutes when she suddenly became cyanosed, vomited and died. The authors stress the need for caution in giving mercurials intravenously to oedematous and wasted patients.

Intravenous mercurial injections—mercupurin—Four deaths occurring immediately after the intravenous injection of mercupurin (an organic compound of mercury containing in each cubic centimetre of solution 39 milligrams of Hg in non-ionizable form, with 3.53 per cent of theophylline) given for congestive heart failure, have been observed by G. Brown, L. Friedfeld, M. Kissin, W. Modell and R. M. Sussman. In each case the fatal dose was 2 cubic centimetres and was not the first dose received by the patient. The first patient had been given mercupurin intravenously on two previous occasions, and each time the injection had given rise to one or more syncopal attacks, the next ten injections were therefore given intramuscularly. For the eleventh injection the intravenous route was again used, death occurred within a minute. The second patient had had numerous intravenous injections before the fatal dose, after most of which brief attacks of dyspnoea had supervened. In the third case forty-two intravenous injections had previously been given without incident; the final injection immediately caused death. The fourth patient gave a history of having received numerous intravenous injections, each of which had been followed by 'unpleasant effects', but four more injections were given without untoward result before the woman received the dose from which she died. The authors state that, in a combined experience of many thousands of intravenous injections of mercurial diuretics, none of them had previously seen a serious reaction.

Phosphorus

Application in chemical warfare—I. M. Rabinowitch, Scientific Adviser on Chemical Warfare, Office of the Director, Civil Air Raid Precautions, Ottawa, has made a comprehensive report on phosphorus lesions, based on information obtained from the British War Office, the British Ministry of Home Security and other official sources and experiences in the laboratories of the Imperial Chemical Industries. Like sulphur, phosphorus exists in allotropic forms, and there are at least five types—red, scarlet red, violet, black and white, the two common forms are the red and white and the contrast in their appearance and other properties is so great that a casual observer would hardly suppose that they are the same element. But red phosphorus does not possess any of the properties with which Rabinowitch's paper is concerned—the capacity to burn and poison—and the following observations refer to white phosphorus only. In peace-time phosphorus is used in a number of industries, and in war is very efficient as a means of creating smoke screens. For its incendiary properties it is used in small arms, in bullets in hand grenades and rifle grenades, in incendiary shells, in trench mortar bombs and in bombs dropped from aeroplanes. Phosphorus is also used in 'tracer' bullets, and it has been incorporated by the Germans into the 312 Mauser machine-gun bullet in sufficient quantity to cause death—and in fact it has caused death—from acute phosphorus poisoning, on which a note is included, pointing out that it was formerly common, before the use of white phosphorus in the manufacture of matches was generally forbidden. As little as 2 milligrams (the amount formerly present in the head of a match) is known to have proved fatal in an infant. The signs and symptoms depend upon whether the phosphorus (a) has been taken by the mouth or (b) has entered the body otherwise, as by a phosphorus-carrying bullet. In the case of ingested phosphorus there may be two phases: (1) primary, due to local irritation of the stomach and intestines, usually two to six hours after ingestion, but less often almost at once, or in rare instances after a delay of twelve to forty-eight hours; (2) secondary, due to absorption of the phosphorus, which may follow the first phase almost at once although usually the interval is from a few days to a few weeks. The clinical picture is one of headache, great prostration, cutaneous haemorrhages, jaundice and hepatic enlargement, which in prolonged cases may diminish in size. The first-aid treatment includes removal of contaminated clothing and of particles of phosphorus with forceps. If the burns are extensive the patient should be evacuated to a hospital. If the burns are small the patient should be evacuated to the nearest first-aid post where the affected parts should be flushed with a warm solution of baking soda or washing soda. First-aid workers should be warned not to use oily or greasy dressings, because they do not possess the necessary facilities to determine whether all the fragments of

phosphorus have been removed. Four stages of the treatment of phosphorus burns are described in detail. The first two stages (first aid and general inactivation) have been briefly mentioned. Stage 3, after the skin has been finally alkalinized, may be occupied by application of dressings by acriflavine (1 in 1000) or other antiseptic, unless it induces eruptions; 'sulpha' pastes and emulsions are satisfactory, but picric and tannic acid and other coagulants are not recommended. In stage 4, immediately healing begins (in from seven to ten days), the affected area may be dressed with boric ointment, which should provide a sound scar.

Barker, M. H., Lindberg, H. A., and Thomas, M. E. (1942) *J. Amer. med. Ass.*, **119**, 1001.

Brown, G., Friedfeld, L., Kissin, M., Modell, W., and Sussman, R. M. (1942) *J. Amer. med. Ass.*, **119**, 1004.

Hoyné, A. L., and Larrimore, G. W. (1941) *J. Amer. med. Ass.*, **117**, 1353.

Lederer, M., and Rosenblatt, P. (1942) *J. Amer. med. Ass.*, **119**, 8.

Meikel, W. C., and Crawford, R. C. (1942) *J. Amer. med. Ass.*, **119**, 770.

Rabinowitch, I. M. (1943) *Canad. med. Ass. J.*, **48**, 291.

Russell, W. O., and Stahl, W. C. (1942) *J. Amer. med. Ass.*, **119**, 1177.

Simon, M. A., and Kaufmann, M. (1943) *Canad. med. Ass. J.*, **48**, 23.

TOXICOLOGY: INDUSTRIAL POISONING

See also B.E.M.P., Vol. XII, p 127, and Cumulative Supplement, Key Nos. 1528–1540.

Prevention of disease in industry

Importance of oral hygiene

Summary of effects of noxious agents.—I Schour and B. G. Sarnat point out that the mouth is an important port of entry for occupational noxious agents. The enamel of the teeth when exposed to injury is incapable of an inflammatory reaction and its response is entirely passive. Acids have a highly deleterious effect upon the enamel owing to their solvent action on the mineral salts. Injury to the dentine is followed by a reaction on the part of the pulp cells, which causes them to form atypical dentine, and often by sclerosis of the dentinal tubules and matrix. Cement, when exposed by shrinkage of the gums, undergoes resorption in response to injury. The alveolar bone responds with a chronic inflammatory reaction. The gums may become chronically inflamed, and shrinkage and pocket formation may occur. It is important to include an inspection of the mouth in any examination of industrial workers. Localized abrasion of the enamel occurs in occupations in which the teeth are used for holding (carpenters, shoemakers, upholsterers) or biting (seamstresses) various objects. Generalized abrasion results from the accumulation on the occlusive surfaces of hard dust such as cement or sand. Decalcification is seen in workers exposed to acid fumes. Workers exposed to sugar dust are said to show a high incidence of dental caries. Staining of the enamel occurs in workers exposed to metal dusts. Occupational pigmentation of the gums is exemplified by the blue line of lead poisoning. Inflammation and ulceration of the mucosa of the mouth and lips may result from inhalation of irritant gases such as ammonia and the secondary infection which ensues. Phosphorus poisoning affects the bone of the jaws. Radium poisoning causes necrosis of bone and from its effect upon the salivary glands, xerostomia. Carcinoma may arise in workers exposed to chronic irritation. Neglect of oral hygiene increases susceptibility to occupational hazards.

Toxic gases

Irritant gases

Fluorides and the production of magnesium.—The industrial hazards involved in the production of magnesium have assumed increased importance because of the demands of war industries for magnesium alloys. C. R. Williams examines from this point of view the various processes concerned. The chief danger arises from the ease with which magnesium and its alloys oxidize at temperatures above their melting-points. This necessitates the use of special oxidation inhibitors and fluxes which may cause air contamination unless precautions are taken. The inhibitors used are sulphuric acid, boric acid, sulphur, soluble fluorides or a combination of these. Fluorides are the fluxes usually employed. The employees in magnesium foundries are thus liable to be exposed to fluorides, magnesium oxide fumes, sulphur dioxide, chromic acid and carbon tetrachloride in addition to dust. The effects of inhaling metallic magnesium are not known. The most important of the contaminants found in magnesium foundries are the fluorides, which occur chiefly in the form of fumes. The amount of hydrogen fluoride gas appears to be negligible. The soluble fluorides are believed to act as protoplasmic poisons. In concentrations exceeding 100 milligrams per 100 cubic metres they have a corrosive action on contact with skin or mucous membranes, shown chiefly by a tingling sensation and running of the nose. The effects are rarely serious enough to be reported to the medical officer. A filter type respirator prevents these symptoms from appearing. Soft paraffin may be inserted into the nose as an added protection. If the furnaces and shake-out operation are kept adequately exhausted the amount of fluorides in the atmosphere can be kept within reasonable limits. Metal fumes are not present in sufficient concentration to produce 'metal fume fever'. Sulphur dioxide concentrations in most foundries are well below 10 parts per million. Chrome poisoning occurs rarely and can be prevented by proper ventilation.

Accidental poisoning by sodium fluoride.—An outbreak of acute sodium fluoride poisoning

in a hospital is described by W. L. Lidbeck, I. B. Hill and J. A. Beeman. After a meal of scrambled eggs, symptoms of poisoning developed in 263 patients and forty-seven of them died. Subsequent inquiries showed that a patient helper, mistaking insect powder for dried milk, had added about 17 pounds of it to 10 gallons of beaten egg. The food was rejected by many of the patients because of a salty or soapy taste. Some complained of numbness of the mouth after eating it. The symptoms set in with abdominal burning and pains soon after the meal. Severe vomiting and diarrhoea followed, and in many cases blood was present in the vomit and stools. General collapse was observed in most of the patients. In some urticaria developed; in some there was a thick mucoid discharge from the mouth and nose. Most deaths took place between two and four hours after the meal. Treatment was of necessity limited to the administration of salt and bicarbonate in water and of stimulants. Magnesium sulphate was given as a purge and probably possessed specific value not appreciated at the time. The insecticide was found to contain 90 per cent of commercial sodium fluoride.

Encephalopathy from lead inhalation.—The risk of lead poisoning run by persons using battery boxes as fuel is illustrated by a case reported by W. D. McNally. A woman aged forty-eight had obtained some battery boxes and in October, 1941 had started burning them in her kitchen range. A short time afterwards she began to have headaches, stiff neck, nausea and vomiting. In November she noticed progressive weakness and loss of appetite. She was admitted to hospital on 12th November, acutely ill, complaining chiefly of headache and tremor of the hands. A lead line was present on the gums. The blood count showed hypochromic anaemia and relative lymphocytosis. The urine contained 0.106 milligram of lead per litre. She was treated with calcium, ammonium chloride and vitamin B and seemed to be improving, when on 1st December she had a convulsion and died. Necropsy findings included thickening of the mitral valve and healed tuberculosis of the upper lobe of the right lung, right tracheo-bronchial glands and parapancreatic glands. Analysis of the tissues for lead yielded the following figures (milligrams per hundred grammes): liver 5.962, kidney 0.62, brain 0.535, pancreas 0.542, adrenals 0.205, bone 5.57. The author urges that careless disposal of battery boxes should be a punishable offence.

Benzene and its homologues

Sources of, and toxicity of, solvents

Effect of volatile solvents in a paint factory.—Esther M. Killick and R. S. F. Schilling have investigated the effects of continued exposure to the vapour of volatile solvents upon workers in a paint factory. Many such volatile substances are used in the paint industry, frequently in the form of complex mixtures or blends. The solvents used in largest quantities were toluene, xylene, butyl acetate, acetone and petroleum solvent; those used in smaller quantities were benzene, ethyl acetate, amyl acetate, solvent naphtha, cellosolve (ethylene glycol monoethyl ether) and butyl alcohol. The probable concentration of the vapours of these solvents in the air of the various workrooms was estimated by the strength of the odour and from the nature of the work being done. The smell of solvents was not overpowering in any part of the factory, not even to workers who were unaccustomed to it, and it was considered likely that any effects produced on the workers would be of a mild chronic type. One case of recognizable poisoning had occurred in the solvent mixing department, in which the odour was strong in the neighbourhood of the plant where the ingredients were weighed. The patient was a man who had been working in the department for eleven months. Two months after beginning work he complained of feeling tired and sleepy, and later of severe headache, dizziness and burning of the skin of the face. Blood examination showed a slight increase in the number of erythrocytes and in the haemoglobin percentage and some leucopenia with a relative lymphocytosis. It was then decided to examine thirty-three other workers exposed to risk. Seven men from a neighbouring metal foundry were examined as a control. The only conspicuous deviation from the normal blood picture among the paint workers was a diminished percentage of polymorphonuclear cells with corresponding increase in lymphocytes. Symptoms of slight narco-sis were common among these workers.

Chlorinated hydrocarbons

Chlorinated naphthalene

Acneiform reactions and acute yellow atrophy.—Thirteen cases of poisoning by chlorinated naphthalene are described by E. Collier. The symptoms may take one of two forms, (1) chloracne of the face, especially the cheeks, and (2) acute yellow atrophy. In the series under consideration twelve were of the former and one was of the latter type. The skin lesions are caused by direct contact with dust or fumes of chlorinated naphthalene, and in a typical case include comedones, papules, pustules and sometimes small cysts. Cleanliness is a prime factor in prevention. The acne cases occurred in one department in which for from three to four months previously technical difficulties had impeded proper exhaust ventilation for the fumes rising from the bath in which chlorinated naphthalene was being melted. In all the cases only the face, excluding forehead and nose, was affected. The thirteenth patient was a woman who had worked for six months in the same department, exposed to the fumes from the bath. Four women working with her were unaffected. The case was diagnosed by the doctor as one of catarrhal jaundice and for the first three weeks of her illness the patient was treated

for this disease; she was then sent to hospital, where she died. At the necropsy the liver was found to weigh only 650 grammes and sections showed acute yellow atrophy.

Injuries from X-rays

Professional workers

Effects of occupational exposure.—At the Section of Radiology of the Royal Society of Medicine a discussion took place on the effects of occupational exposure to X-rays and to radioactive substances. J. R. Nuttall drew attention to the observation which so far as he knew had not been described, namely of the curious phenomenon of acute irradiation tiredness, physical and mental, which may occur after comparatively large exposures to irradiation. At the Manchester Radium Institute the phenomenon had been regarded as being evidence of excessive exposure. Such tiredness was not constant in all workers and might be modified by conditions of temperature and ventilation. The old Manchester Radium Institute was small and badly protected; there had been several cases of skin lesions occurring in workers in the building, and at least one member of the medical staff had abandoned radium work on account of serious blood changes which showed the prodromal signs of aplastic anaemia. The average total leucocyte count of all workers fell to 4,300, with individual low counts of 3,000. In 1933 the Institute moved to new quarters with efficient protection so that the average total leucocyte count at first rose to 4,400 and then to 6,000, at which level it has since remained. Workers in X-ray departments who use completely protected tubes operating at 240 kv can safely carry on with a leucocyte count of 6,000 although the figure is lower than that which is regarded as normal. There is, however, room for further regulations with regard to the clinical use of radium because, although up to a point there is comparative safety, a very little increase in exposure undoubtedly causes leucopenia. J. C. Mottram pointed out that irradiation changes the hereditary function of cells in two ways, by causing chromosomal aberrations and by producing gene mutations. The latter mutations are the common spontaneous forms which were known long before Muller discovered that X-rays cause mutations. S. Russ discussed what is the threshold of safety of radon in the air, and concluded that for safety it should be recommended that a concentration of radon of 10^{-10} curie per litre in the air should not be exceeded. Janet M. Vaughan, from a review of the available evidence, concludes that external irradiations from X-rays or radium have not any effect on the erythrocytes or haemoglobin level of workers who already have a satisfactory blood count. She also adds that, provided reasonable precautions are taken, X-rays and probably external irradiation with radium are also without effect upon the leucocyte count in a subject with a normal leucocyte picture. On the other hand internal irradiation with radioactive substances—as was reported years ago by H. S. Martland and as set out recently in the Factories (Luminising, 'Health and Safety Provisions') Order—is a serious industrial hazard.

EDITORIAL COMMENTARY—New Dangers in Industry

It is difficult to keep pace with the dangers occurring in the chemical, metallurgical, munitions, aircraft, ceramics, textile, cellulose lacquer and moulded plastics industries. The present rate of industrial development demands the frequent discovery of new materials. The substances produced rapidly become indispensable but their properties may remain for a long time insufficiently understood. Some of them are dangerous under certain conditions: but on several occasions the degree of the danger has not been realized until a fatal accident has occurred.

Many new alloys which entail the use of unusual metals are being developed. Beryllium steel has such remarkably valuable properties that it will doubtless receive much commercial attention. In the preparation of this alloy a certain amount of dust is continually given off by the molten salt electrolytic baths. This dust consists of sodium silico-fluoride, barium fluoride, beryllium oxide and beryllium fluoride. The dusts of all these compounds are known to be toxic to animals. What will they do to man? Other metals, rare or unknown a few years ago, are now assuming commercial importance, especially indium, rhodium and titanium. Whereas little is known concerning the toxicity of these substances, it can be stated definitely that thallium and cadmium fumes are extremely toxic.

It is well known that the physical form in which a metallic compound exists in the atmosphere may determine its toxicity. Thus, zinc oxide may produce toxic effects when inhaled as fume and yet it may be relatively inert when inhaled as dust. Lead absorption is always greatest among those exposed to freshly formed lead fume. Thus, in the occupation of lead burning performed with an oxy-acetylene flame 100 per cent of men absorb lead, whereas in spray painting only 44 per cent do so.

In the case of chromium compounds toxicity is determined by the valency of the metallic radicle. Chromium plating exposes the worker to spray or mist which is carried into the air by bursting bubbles over the plating vats. Hexavalent chromium compounds are used and they attack the skin through the slightest abrasion, causing dermatitis and the well-known chrome holes or chrome ulcers. In addition, perforation of the nasal septum occurs in more than half the number of men exposed. Now this toxic action is confined to the compounds of hexavalent chromium. Trivalent chromium salts such as the phosphate and carbonate salts have no toxic action.

The original conception of chronic benzene poisoning has been found to be an oversimplification based on insufficient human material. It was thought that the attack on the

bone marrow was always destructive, affecting first the platelets, then the granular leucocytes and finally the erythrocytes. The settled belief grew up that a diagnosis of benzene poisoning is not justified unless the blood picture shows an aplastic anaemia associated with a leucopenia, and a relative lymphocytosis; that a leucopenia is more important in diagnosis than a low red cell count; that cases of benzene poisoning invariably show purpuric manifestations associated with bleeding gums, epistaxis or menorrhagia; that the spleen is never enlarged in these cases; that at necropsy the bone marrow is always in a state of aplasia; that young women are more susceptible than men to the vapour of benzene; and that a concentration of 100 parts per million or less in the air may be considered safe.

Although it is true that some advanced cases do show many of these features, we now know that erythrocytosis, leucocytosis, eosinophilia and even leukaemia may be encountered. The evidence that chronic exposure to benzene produces leukaemia in human beings is still incomplete, but it is accumulating rapidly and to a volume which commands serious consideration. It is best to regard as unsafe any concentration of benzene greater than zero inhaled over a long period. The presence in a workshop of the characteristic odour of the solvent is a danger signal. Benzene poisoning could best be prevented by abandoning its use as a solvent. From medical investigators all over the world comes the plea to use one of the many harmless substitutes. Certainly benzene should be used only under the best conditions of ventilation, local or general, with periodical examination of the exposed workers.

Tri-*ortho*-cresyl phosphate, known to be poisonous since 1899, has now caused trouble in industry. It is used in the plastics industry as a plasticizer, that is a substance added to render a plastic material more pliable. The clinical picture of tri-*ortho*-cresyl phosphate poisoning is that of a polyneuritis with flaccid paralysis of the distal muscles of the upper and lower extremities. Slow but complete recovery usually occurs. Since 1939 three men manufacturing this substance have been poisoned in a chemical works. All three worked in a room about 25 feet long, 12 feet wide and 12 feet high, which, owing to black-out regulations, was totally enclosed during the hours of darkness, although it was provided with a roof vent. During the day-time doors and windows were open. The men worked at wash-tanks which were roughly cubic vessels of about five feet side, with a partially open top. The closed-in portion of the top supported the various fittings, one of these being a six-inch vent pipe extending through the roof to the open air. Crude tricresyl phosphate entered these tanks at a temperature of approximately 60° C. At this stage it contained hydrochloric acid which gave it an unpleasant irritating odour. However, it was immediately cooled down by treatment with an equal volume of cold water, this operation being carried out by opening a valve and shutting it at the appropriate moment. The washing was automatic but it was nevertheless possible for the men to inhale fumes from the tank. The cold tricresyl phosphate is of low volatility, having a small vapour pressure at ordinary temperatures. The *ortho*-isomer content of the finished product was about 60 per cent. Two of the men affected recovered completely in periods of ten and twelve months respectively, the third is still making slow progress but is not entirely well at the time of writing, which is twenty months after the onset of symptoms. In order to try to prevent further harm, the firm employing the men fitted the wash-tank room with ventilators and a fan. The tanks were closed in and the vent fitted with injectors so that the vapours might be quickly transferred to the open air.

In the last two decades or so a great new aliphatic chemical industry has grown up, which is already bigger than the coal-tar or aromatic chemical industry. One result of this has been the rapid introduction of a host of new solvents including ethylene chlorohydrin, dioxan, cellosolve, cellosolve acetate, methyl cellosolve, butyl cellosolve, carbitol (diethylene glycol mono-ethyl ether) and butyl carbitol. The first two of these substances have already caused poisoning in man, and it is essential that the others of the group be watched carefully lest toxic symptoms occur in workers using them. DONALD HUNTER

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TRENCH FEVER

See also B.E.M.P., Vol. XII, p. 236; and Cumulative Supplement, Key No. 1548.

Clinical picture and prognosis

Types

Symptoms and treatment.—A. Hurst remarks that trench fever has long been endemic in Poland and persists there to the present day. The causative organism, *Rickettsia quintana*,

inhabits the guts of lice and is excreted in their faeces; it is transmitted to human beings when a contaminated area of skin is scratched. The incubation period is from fifteen to twenty-five days. The onset is usually sudden, with severe headache followed by pain in the back and later in the legs; the shins are always tender. The temperature rises rapidly to 102° F. or 104° F., but the pulse rate rises only slightly. In the short form the temperature falls to normal on the third or fourth day without subjective improvement, and after a few hours rises again, falling finally with relief of symptoms after another period of from two to five days. In the long type the fever is periodic and relapses occur about every five days for a number of weeks. Prophylaxis implies delousing. No specific treatment is known. It is important to get the patient out of hospital as soon as possible, sending him to convalesce under good conditions.

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TRICHINIASIS

See also B.E.M.P., Vol. XII, p. 241; and Cumulative Supplement, Key No. 1549.

Clinical picture

Psychotic factors

An interesting fatal case—K. Stern and T. E. Dancey report a fatal case of trichiniasis in a woman, aged thirty-five, whose maternal grandmother, great-uncle and sister had been admitted to mental hospitals, and whose maternal grandfather had attempted suicide on three occasions; a nephew had also committed suicide. It is known that nervous symptoms may complicate trichiniasis, but the case quoted must be exceptional in that a symptomatic psychosis, without any focal signs, dominated the clinical picture of trichiniasis infestation. The clinical severity was in striking contrast to the scarcity of parasites found anatomically, the larvae being found only in serial sections. Another point of interest is that the patient showed signs of acute mental breakdown a few days before the underlying infestation became apparent, this being in agreement with Kraepelin's classical dictum that the symptomatic psychotic manifestations of an internal disease may appear before the disease itself.

Diagnosis and differential diagnosis

Intradermal injection of antigen

Positive reactions after antigen sensitization—Bessie Baron and M. Brunner have carried out experiments to determine whether or not the skin test doses of trichinella antigen used to detect *Trichinella spiralis* infestation can sensitize patients to the antigen. Three different extracts of *T. spiralis* were prepared by various methods and were used in three series of six persons. The subjects were atopic patients attending a clinic for allergic diseases, and ranging in age from four to forty-four years. Only those giving a negative reaction to an intracutaneous injection of antigen were selected for the experiments. Injections were given to each subject at intervals of from seven to fourteen days over a period of from four to twenty weeks. With the development of sensitivity a positive reaction (erythema, wheal formation and itching) resulted from the intracutaneous test. Sensitivity, as shown by such a reaction, was induced in ten (56 per cent) of the subjects, reactions occurring after a number of doses varying from three to nine. The induced positive reactions were found to be transferable to normal skin. The method used was to inject intradermally 0.05 millilitre of the serum of an artificially sensitized individual at several sites in the skin of a normal person and to test the sites of injection from three to seven days later. Control tests were made on the skin adjacent to the sensitized sites. Similar tests carried out with *Ascaris* extracts demonstrated the existence of a common antigen in *Ascaris* and *Trichinella*. The results of these experiments indicate that the diagnostic value of the trichinella test diminishes with repetition.

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TROPICAL DISEASES. GENERAL SURVEY

See also B.E.M.P., Vol. XII, p. 247.

Minor tropical diseases

Mossy foot

Clinical picture and diagnosis.—F. W. Simson, C. Harington and J. Barnetson of the Department of Pathology, South African Institute for Medical Research, Johannesburg, report six cases of chromoblastomycosis (dermatitis verrucosa, mossy foot), the causal organism of which was isolated and described by both C. G. Lane and E. M. Medlar in 1915. The term, chromoblastomycosis, was introduced by O. da Fonseca in 1922. In 1941 more than a hundred cases were analyzed by F. D. Weidman and L. H. Rosenthal. It is a chronic fungal granuloma widespread but without racial predilection or immunity, occurs chiefly in adult males in the lower extremity and may be associated with several variants of a particular fungus which may exist as a saprophyte. The authors' cases are the first published in South Africa; it appears to have little effect on the general health, but is slowly progressive and gives rise to gross disfigurement of the affected part. The diagnosis is established by the histological appearance of a tuberculoid reaction and the presence of rounded brown bodies resembling yeast cells, or by isolation of the fungus from one of the nodules. In a typical case a papillomatous nodule appears on the foot or on lower part of the leg; usually single at first the nodules later become

multiple. They are easily affected by trauma, and when injured they are prone to secondary infection and ulceration.

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TRYPANOSOMIASIS

See also B.E.M.P., Vol. XII, p. 263; and Cumulative Supplement, Key No. 1553.

Treatment

Curative

Diamidine compounds, antrypol and tryparsamide.—A report on the treatment of sleeping sickness due to *Trypanosoma gambiense* is issued by E. M. Lourie. In a group of 3,197 patients, 5 per cent showed serious symptoms, the remainder were representative of earlier cases. The patients were generally very poor and undernourished, subsisting almost entirely on rice. The majority were treated by antrypol and tryparsamide, alone or in combination; a few were treated by the aromatic diamidines, stilbamidine, pentamidine and propamidine. The intravenous route was mainly used, the intramuscular route being used occasionally. With antrypol and tryparsamide, toxic effects appeared in about 20 per cent and 10 per cent of patients respectively. In from about 3 to 5 per cent in each group the symptoms were serious; the mortality was under 1 per cent. Under combined treatment by three injections of antrypol 1 gramme (15 grains), with five subsequent injections of tryparsamide 2 grammes (30 grains), at five-day intervals, the incidence of toxic reactions rose to 35 per cent, 15 per cent of the cases being serious, with a mortality of 5 per cent. Very late cases are omitted from these figures; the death rate among such cases is considerably higher. Other combinations of drugs, however, for example one dose of antrypol with nine doses of tryparsamide, showed a much lower incidence of reactions. The incidence of serious visual disturbances appeared to be related directly to the cell content of the cerebrospinal fluid. With the diamidines, a sharp but transient fall of blood pressure was the most conspicuous immediate effect, accompanied by severe and sometimes alarming collapse. No patient died, however. Late toxic effects, or visual or other manifestations, were not observed. The dose given in the first few cases was 1 milligram per kilogram; later all the adults received 50 milligrams. The diamidine compounds possess the advantage over antrypol and tryparsamide that injections can be given daily. In early cases the symptoms responded equally well to all the treatments used, in the later cases the patients appeared to benefit more from administration of tryparsamide. The percentages of patients (excluding advanced cases) who became symptom-free and remained so at the time of the later examination (from twelve to twenty months later) was equal (90 to 95) for tryparsamide, pentamidine and propamidine, when full courses were given; for stilbamidine the percentage averaged only 45. In advanced cases the survival (with health) rate was much better (58 per cent) with tryparsamide than with pentamidine (11 per cent) or with other diamidines (0 per cent). Decrease of the cell content of the cerebrospinal fluid occurred in a similar proportion of the patients who were treated by the different drugs.

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TUBERCULOSIS

See also B.E.M.P., Vol. XII, p. 286; and Cumulative Supplement, Key No. 1554

Epidemiology

Incidence of infection

In the adult population of Harlem.—As A. B. Robins points out, mortality statistics do not accurately reflect the incidence of pulmonary tuberculosis. The prevalence of the disease in a given population can be ascertained only by X-ray examination of all its members; since this is impracticable, sampling methods must be employed. In an attempt to determine the incidence in the adult population of the Harlem area of New York, the author has re-examined 8,731 recipients of home relief who had previously been examined by X-rays with negative results. The average interval between the two X-ray examinations was 14.2 months. Negroes constituted 86.2 per cent of the group. Twenty-five cases of pulmonary tuberculosis were discovered, fourteen in females. More than two-thirds of the patients were over thirty when the diagnosis was made. In eighteen the lesion was situated in the right lung, in five in the left lung; in one patient both lungs were affected. The predilection of the infection for the right lung was more pronounced in females. The history was negative for known contact in eleven of sixteen cases in which a history was obtained. Only nine of the patients gave a history of symptoms prior to the discovery of the lesion by X-ray examination. In six the symptoms were of less than three months' duration. Eighteen of the patients have been observed subsequently. Seven deaths have occurred, all in negroes, five of them females. The average interval between negative X-ray findings and death was 20.1 months, and between positive X-ray findings and death, eight months. The incidence of tuberculosis in the entire group was 2.2 per thousand; in a control group consisting of 4,000 individuals who failed to return for a

second X-ray examination, the incidence was found, by checking the names against the central register for tuberculosis, to be 2·4 per thousand; this figure confirmed the representative character of the sample.

In American college students—C. E. Lyght presents a second five-year review (1937–41) of tuberculosis in American college students, amongst whom it remains first on the list of causes of death, although it is reduced to the seventh cause among the general population. Three hundred and four colleges now sponsor tuberculosis investigations on their students under the auspices of the Tuberculosis Committee. Tuberculin testing was used in 149,744 individuals during the five-year period, the tests being done mainly by the Mantoux method but in some colleges the von Pirquet or patch test was used. The Tuberculosis Committee favours the former method, a minute dose is given first to weed out the highly allergic few, and a larger dose is given afterwards to the many non-reactors. The percentage of positive reactions was 20·7, compared with 27·3 in the first five-year period. Annual radiographical examination of all reactors is urged, and is at present carried out in 28 per cent of all the colleges. A few colleges have adopted mass (miniature) radiography, but the tuberculin test is preferred by the author for routine use, because it gives a more exact measure of the tuberculous process. An increasing number of colleges insist on examination of all persons who handle food, and also offer examination to their teaching staff. In the colleges which participated in the survey the total enrolment for the five years amounted to 1,850,755 members and, among these, 3,523 new cases of tuberculosis were discovered. The figures imply that thousands of cases of tuberculosis, many of them infectious, are being harboured in American colleges. Abysmal ignorance among people who should know better still results in much opposition to work on tuberculosis being carried out in colleges, but an encouraging advance nevertheless has taken place during the last five years.

Relative incidence in age groups

Survey of households—R. G. Hahn has studied 414 households each including one tuberculous member and a total of 1,909 persons. The primary case was that of the husband (father) in 229 families, the wife (mother) in 113 and one of the offspring in 72. Contacts were kept under observation for from one to five years from the beginning of the period of exposure to infection. The numbers of contacts who became infected were as follows. (1) When the husband (father) was the source of infection clinical tuberculosis developed in 7·9 per cent of the wives, 2·2 per cent of children under ten and 5·9 per cent of those over ten years of age. The percentages in whom asymptomatic tuberculosis was detected by X-ray or estimated to have occurred were 11·8 among the wives, 5·3 among the children under ten and 3·2 among the children over ten. (2) When the primary case was the wife (mother) clinical tuberculosis developed in 5·3 per cent of husbands, 5·1 per cent of children under ten and 5·7 of children over ten. Asymptomatic disease was detected or estimated in 18·6, 3·4 and 6·8 per cent respectively. (3) When the primary case was that of a son or daughter, clinical infection occurred in 4·2 per cent of the fathers, 4·2 per cent of the mothers and 5·8 per cent of the children over ten. Asymptomatic tuberculosis was observed or estimated in 8·3 per cent of fathers, 6·9 per cent of mothers and 5·2 per cent of children over ten. No child under ten developed tuberculosis. Intimate contact such as that which occurs in households is associated with a higher risk of infection than that existing in larger groups of people in which contact is less close. Thus among the employees of an insurance company, examination during two five-year periods revealed tuberculosis infection in 2·27 and 1·18 per cent respectively.

Immunity and allergy

Factors governing resistance

Effect of low oxygen tension.—A. R. Rich and R. H. Follis, Jun. have investigated the effect of low oxygen tension upon experimental tuberculosis. They argue that reduction of the oxygen supply is likely to have a deleterious effect upon the respiration and upon multiplication of the tubercle bacillus. Rabbits and guinea-pigs were kept in a specially designed chamber in which any desired oxygen level could be maintained. As a control, an equal number of animals were kept in open cages in the same room. All were fed alike, and each animal was artificially infected with an equal dose of virulent tubercle bacilli. All the animals were killed after three or four weeks and the organs were examined for tuberculous lesions, which were graded in five categories. It was found that in animals kept in an atmosphere containing not more than 10 volumes of oxygen per cent the lesions were distinctly less advanced than in the controls. When the oxygen content of the chamber was raised to 20 volumes per cent no difference was found between the animals kept in the chamber and the controls. The beneficial effects of collapse and high altitude therapy may be related to the reduced oxygen tension, which may also account for the high resistance of the foetus to tuberculous infection.

Tuberculous infection in early childhood.—H. C. Cameron points out that the idea that tuberculous infection in early childhood is particularly virulent is being relinquished. It is realized today that although infection can be of grave significance it is usually controlled with success, and a primary tuberculous lesion in a child is far less serious than in an adult. The latent period before sensitivity to the tubercle bacillus develops gives time for encapsulation and fibrosis to occur. Once sensitivity is present renewed infection, either exogenous or endogenous, will give rise to very considerably more tissue reaction which is of an allergic character. The cutaneous tests for tuberculosis are examples of this allergic reaction in sensitized tissues. The allergic response provides the drastic remedy required when danger is

renewed and when milder methods have failed. Primary infection may take place in the lung, eye, ear, nose, throat, skin or intestine. In the last-named situation it is in the main bovine and milk-borne. Young children should never be given raw milk. Renewed infection, for the reasons given above, is associated with severe and sometimes fatal reactions. Danger is greatest at two periods, namely immediately after the primary infection and in adolescence. In very young children the danger of meningitis is great; it occurs as a rule between the fourth and sixteenth week after the primary infection. Renewed infection at puberty may be either exogenous or endogenous; the relative frequency is unknown. The degree of immunity to tuberculosis developed as the result of the primary infection is not enough to prevent reinfection from without. In the lung the response takes the form of phthisis with caseation, ulceration and fibrosis in variable proportion. Skin tests furnish the best index of tuberculous infection. Children should be tested at intervals throughout their childhood, and those who react positively should be examined by X-rays periodically, to examine in this manner those who react negatively is unnecessary and wasteful. Protective inoculation is still in the experimental stage. Chief reliance must be placed on the detection, notification and supervision of infected adults, examination of all child contacts and supervision of all those who are found to be infected.

Morbid anatomy

Localized lesions

Results of treatment by Promin—W. H. Tytler and A. D. Lapp have used 5 per cent promin (promanide) as a local application for superficial tuberculous lesions and report results which they think justify further trial of the drug in suitable cases. The vehicle used was a stiff tragacanth jelly and no attempt was made to sterilize the preparation, but it is pointed out that unsterilized preparations are not regarded as ideal for injection into closed cavities, because of possible danger from viable spores. Ten patients have been treated; in only four were tubercle bacilli isolated from the pus, and in one a pure growth of *Staphylococcus aureus* was obtained. The opinion was formed that in all the cases improvement was greater or more rapid than could have been expected with older methods of treatment. In two cases a rise of temperature occurred on the day after an injection, but this may have been caused by disturbance of the abscess.

Diagnosis

Cultivation and guinea-pig inoculation

Effect of blood charcoal in cultivation—F. Nassau found that the addition of 1 per cent of blood charcoal to solid and liquid media resulted in a definite increase of the growth of the human type of the tubercle bacillus; on the whole the colonies of bacilli appeared sooner and in greater numbers on the charcoal medium than on controls. The charcoal seems to act not only as a metabolic but also as a reproductive stimulant to the growth of tubercle bacilli on the media employed. Blood charcoal was added to half of every batch of media prepared for routine work, and in the course of two months about 250 cultures were made from various pathological specimens such as sputum, gastric contents, urine, pus and laryngeal swabs.

Serial inoculation—J. F. Pottenger, of the Pottenger Sanatorium, Monrovia, California, returns to his advocacy of serial inoculation of guinea-pigs with sputum for the more accurate diagnosis of infection by *Mycobacterium tuberculosis*. Since 1935 five 3-day specimens of sputum have been inoculated serially as a routine. Each of a series of five 3-day specimens is digested with equal parts of 0.5 per cent sodium hydroxide or, if the quantity collected is large, one drop of 20 per cent sodium hydroxide is added to each four cubic centimetres of the specimen. The mixture is shaken and set at 37° C. for two hours, which reduces markedly the virulence of the contaminating organisms. The usual sequence of the site of inoculation is left axilla, right axilla, left inguinal region, right inguinal region, left abdominal wall and right abdominal wall. When intraperitoneal inoculation is used it is given with the first inoculum so that, in case of early death of the animal, other inoculations are not lost. The results of serial inoculation of guinea-pigs was found to be more satisfactory than was a single pool inoculation. Two positive results which occurred in 342 consecutive positive animal tests were questioned, and were not confirmed by repeated tests, the patients did not show any clinical evidence of tuberculosis. Serial inoculation is especially useful in cases of doubtful diagnosis and in patients in whom minimal lesions are masked by changes in the lungs, as in bronchiectasis.

Cameron, H. C. (1943) *Practitioner*, **150**, 291.

Hahn, R. G. (1943) *Amer. Rev. Tuberc.*, **47**, 316.

Lyght, C. E. (1942) *Amer. Rev. Tuberc.*, **46**, 227.

Nassau, E. (1942) *J. Path. Bact.*, **54**, 443.

Pottenger, J. F. (1942) *Amer. J. clin. Path.*, **12**, 412.

Rich, A. R., and Follis, R. H., Jun. (1942) *Johns Hopk. Hosp. Bull.*, **71**, 345.

Robins, A. B. (1943) *Amer. Rev. Tuberc.*, **47**, 1.

Tytler, W. H., and Lapp, A. D. (1942) *Brit. med. J.*, **2**, 748.

TUMOURS

See also B.E.M.P., Vol. XII, p. 313; and Cumulative Supplement, Key No. 1557.

Morbid anatomy

Microscopic features

Liposarcoma.—R. B. Moreland and W. L. McNamara report nine cases of the rare neoplasm, liposarcoma, encountered in a series of 16,000 patients with tumours. The sites of origin were as follows: gluteal region and thigh, four cases; retroperitoneal tissue, three cases; chest wall, one case; scapular region, one case. The patients were all men, aged from thirty-eight to sixty-eight years; the length of the history varied from three months to fifteen years. Several patients had previously undergone one or more operations. Growth of the tumour may be rapid or slow; in two cases the swelling had first remained stationary and had then begun to grow rapidly. A liposarcoma may be encapsulated and shell out readily at operation but, despite this fact, it is decidedly malignant, and tends to recur locally and to metastasize early. Of the nine cases in the above series, two were inoperable. Of the seven patients who were operated upon, two died within fifteen months, one as a result of recurrence, the other after operation for recurrence, five were alive and well at periods ranging from twenty months to five years, although in one case removal of a retroperitoneal tumour was known to be incomplete. The diagnosis of liposarcoma can be made only by histological examination which shows fat cells in all stages of development. Treatment is surgical; radiotherapy was used in some of the above cases without effect.

Moreland, R. B., and McNamara, W. L. (1942) *Arch. Surg., Chicago*, **45**, 164.

TYPHUS FEVERS

See also B.E.M.P., Vol XII, p. 325; and Cumulative Supplement, Key Nos. 1558–1560.

Fevers of the typhus group

Classification

Antigenic types—A. Felix classifies the typhus group of fevers according to the antigenic type of the causal *Rickettsia* into three immunological subgroups. The first, which includes classical louse-borne epidemic typhus, is known as *OX* 19, the second as *OX* K and the third is a miscellaneous collection, probably of various types. Owing to the great difficulty of obtaining pure strains of *Rickettsia* in sufficient quantities (a difficulty now being overcome, thanks to the introduction of better methods of cultivation) serological studies have been based upon the fact that *Rickettsia* and *Proteus* X contain a corresponding heat-stable antigen. *Rickettsiae* also contain a heat-labile antigen which not only acts as a toxin but inhibits the interaction between the *O* (heat-stable) antigen and its corresponding antibody and thus protects the *Rickettsia* against the action of the latter. These two antigens, and possibly others as yet unknown, play essential parts in the production of immunity to typhus fever. Specific serums have so far proved ineffective in treatment. Convalescent serum cannot be obtained at an early enough stage of defervescence to contain more than an insignificant quantity of the *O* antibody, of which the titre is highest just before or just after the temperature falls, and rapidly decreases. Animal serums so far prepared are no more efficacious, but the serum of horses immunized against *Proteus* X seems likely to prove more useful. Vaccines have been prepared by various methods and encouraging results of prophylactic immunization have been reported.

Aetiology

Rickettsial diseases in Australia.—The importance of rickettsial diseases as a public health problem in Australia is not great, but a study of the cases has brought to light facts which may be helpful in tackling such diseases elsewhere. F. M. Burnet in his Bancroft memorial lecture states that these diseases were probably introduced into Australia when the second fleet of convict ships arrived in Sydney in 1780. In several of the ships epidemics of classical typhus fever occurred, but conditions ashore were unfavourable to its spread and it quickly died out. Sporadic cases have occurred in Australia ever since, and a comparatively large epidemic broke out in Toowoomba in 1926; it was probably related to one of the increases in mouse population which recur at intervals in Australia. Scrub typhus (*tsutsugamushi*), another rickettsial disease conveyed by a mite, occurs in swampy country; serum from infected people agglutinates *Proteus* X K 19. 'Q' fever was recognized a few years ago in slaughter-house workers in Brisbane; it is a mild disease, apparently conveyed by cattle ticks and acquired by inhaling dust containing the ticks' dried faeces. Similar cases have occurred among members of a laboratory staff at Melbourne, in whom infection was thought to have been acquired by inhalation of infective dust while taking guinea-pigs' temperatures.

Epidemic or louse-borne typhus fever

Clinical picture and course

Observations made in a prison camp.—C. Donald and P. B. Barker write from a prison camp in Germany to describe their observations on a series of twenty-one cases of typhus fever occurring in the camp. Sixteen of the patients had been employed in handling clothing at the camp disinfecter. In two cases only was it possible to determine the incubation period, which was, as usual, from twelve to fourteen days. In the milder cases fever was the initial symptom and the patients felt quite well for the first three or four days, despite temperatures of about 102° F. In the more severe cases the onset resembled influenza, with headache, sore throat and shivering. One patient had acute abdominal pain and vomited twice, and was operated

on for supposed appendicitis. In the pre-eruptive stage the patients' general appearance somewhat resembled that of measles, with redness of the conjunctivae and flushing with slight cyanosis of the face. The tongue was dry and furred, the facial expression was worried, and speech was sluggish. Some patients were delirious, all became increasingly drowsy. Acute dyspnoea usually occurred towards the end of this phase and a few crepitations were audible. The problem of diagnosis during the pre-eruptive stage, and in milder cases without rash, is an urgent one. Points in favour of typhus fever are certain occupations, presence of lice, typical facies and acute dyspnoea without proportionate signs; the blood picture shows polycythaemia with leucocytosis at first, the haemoglobin and erythrocyte levels falling rapidly when the haemorrhagic rash comes out; the spots, if present, are more numerous than in typhoid fever. The Weil-Felix test is not positive before the rash comes out and therefore is not of any use in early diagnosis; it was positive in all cases after the seventh day. The rash appeared usually on the sixth day, and in 19 per cent of patients occurred on the face; it became haemorrhagic within a few days. Treatment by sulphonamides and antipyretics had no effect. Good nursing is essential; complications included bed-sores, transient optic neuritis, lung abscess, partial atelectasis, persistent vertigo, persistent ulnar neuritis and persistent hypertension. Three (14.28 per cent) of the patients died. Attention is drawn to the close similarity between typhus fever and epidemic encephalitis.

Non-epidemic or epizootic typhus fevers

Tick-typhus

Toxaemic signs in guinea-pigs.—B. de Meillon of the South African Institute for Medical Research discusses the position concerning the toxin isolated from the ova of ticks, and quotes B. Oswald as questioning the identity of the egg toxin with that of tick paralysis which is known to occur in South Africa in association with the ticks *Ixodes pilosus* and *I. rubicundus*. De Meillon concludes that a toxin is present in the ova of the following ticks: *Rhipicephalus evertsi*, *Boophilus decoloratus*, and *Haemaphysalis leachi* from Johannesburg, and *H. leachi* from Lourenço Marques; it is probable that the toxin is present in the eggs of all ticks and from the moment they are deposited until they begin to hatch; the toxin is a protein which generally can be salted out with sodium sulphate at 57° C; the supernatant fluid obtained from spinning out the protein after salting out with sodium sulphate contains a toxic principle which causes fever in guinea-pigs but without any of the signs typical of toxæmia produced by protein precipitate, the signs of toxæmia produced in guinea-pigs by subcutaneous injection of the toxin from the tick's eggs are (a) almost immediate fever—many guinea-pigs given large doses collapse with a low temperature on the second or third day; (b) loss of appetite; (c) loss of weight, (d) diarrhoea; (e) hyperaesthesia; (f) disinclination to move; (g) staring coat. In one guinea-pig only was paralysis noted, and then forty-eight days after injection. At the site of injection an indurated, ulcerated area may arise; but this is not constant. Guinea-pigs recovering from the effects of egg toxin are not immune to tick bite fever. The toxin of tick paralysis is not closely related to that obtained from the ova of ticks

Burnet, F. M. (1942) *Med. J. Aust.*, **2**, 129.

Donald, C., and Barker, P. B. (1942) *Brit. med. J.*, **2**, 333.

Felix, A. (1942) *Brit. med. J.*, **2**, 597.

de Meillon, B. (1942) *S. Afr. J. med. Sci.*, **7**, 226.

Oswald, B. (1938) *Ann. parasit. hum. comp.*, **16**, 548.

ULCERS

Treatment

Surgical treatment

Skin grafting in chronic ulceration of the leg.—Chronic ulceration of the leg results from ischaemia which, as R. E. Heller observes, may originate in any disorder of the circulation; secondary infection supervenes which further disturbs nutrition by the production of scar tissue. Treatment must aim at correction of the causal circulatory disorder as well as be directed to the local condition. If simple supporting bandages in addition to treatment of the cause fail to promote steady healing, skin grafting, with or without preliminary excision, should be considered. The rate of healing may be measured by tracing the outline of the ulcer on Cellophane each time the dressing is changed; it varies in direct proportion to the original size of the ulcer.

Heller, R. E. (1943) *Surg. Gynec. Obstet.*, **76**, 77.

UNDULANT FEVER (MELITENSIS and Suis Types)

See also B.E.M.P., Vol. XII, p. 361.

Aetiology

Sources of infection in man

Infected cows and pigs.—An account of an epidemic of brucellosis (undulant fever) is given by I. H. Borts, D. M. Harris, M. F. Joynt, J. R. Jennings and C. F. Jordan. During late August and early September, 1941 nine cases yielding positive agglutination tests for brucellosis were reported from Marcus, a town of 1,200 inhabitants in Iowa. Four cases occurred in

one family. On inquiry it was elicited that all the patients had been supplied by the same dairyman, who delivered only raw milk. On 10th September arrangements were made to have cows tested for evidence of infectious abortion, and orders were given in the meantime for all milk to be pasteurized. Despite this precaution new cases continued to occur up to March, 1942 owing probably to the length of the incubation period, which may be as much as four months. Agglutination tests were carried out on people who had consumed milk from the suspected dairy and seventy-seven gave positive results. To reveal latent or subclinical cases 237 school children were also tested and twelve gave positive reactions. Intradermal and opsonocytaphagic tests were carried out on other school groups and a number of positive reactions was obtained. Most of the patients suffering from brucellosis were ill for six or eight weeks. Only one case was severe and no deaths occurred. Blood cultures were obtained from twenty-nine patients and *Brucella suis* was isolated from thirteen (45 per cent). Among forty-three cows belonging to the suspected dairy three strongly positive reactors and one doubtful positive were discovered. Direct culture of the cream from these cows yielded growths of *B. suis* in two cases, and guinea-pig inoculations gave three positive results. None of the cows supplying other dairies in the town were positive reactors. Inspection of the affected farm showed that the cows were allowed to mingle freely with the pigs, and of the twenty-four sows eleven gave positive and three doubtful agglutination reactions when tested for infective abortion. The treatment of the patients consisted in prolonged rest in bed and administration of brucellin. This preparation, the filtrate from cultures of brucella organisms, was given subcutaneously in increasing doses from every three to every five days until no febrile reaction followed the injection of 1 cubic centimetre. Three patients who had severe reactions after the initial injections were given sulphonamides instead, but in general these drugs were avoided because of the secondary anaemia shown by most of the patients.

Borts, I. H., Harris, D. M., Joynt, M. F., Jennings, J. R., and Jordan, C. F.
(1943) *J. Amer. med. Ass.* **121**, 319

URAEMIA

See also B.E.M.P., Vol. XII, p. 379.

Aetiology

Inhibition of formation and excretion of urine

Anuria after sulphonamide therapy—J. Carson and G. S. Smith describe the case of a man, aged forty-three, who was admitted to hospital with lobar pneumonia, after he had been treated for five days by sulphapyridine of which he had received a total of 22 grammes (330 grains). On the day before admission to hospital the urine had become scanty and blood-stained, and the drug was discontinued; since then no more urine had been passed. On admission severe pain was present in the hypogastric region and over the tip of the penis. The skin and mucous membranes were pale, the tongue was dry and furred. The abdomen was slightly retracted and was tender over the lower half. On catheterization the bladder was found to be empty. Fluids were given freely by mouth and intravenously. The patient became slightly drowsy but remained conscious until shortly before death, which took place after a period of sixty hours of anuria, and forty hours after admission to hospital. Three hours before death the blood urea was 100 milligrammes per 100 cubic centimetres. At necropsy the kidneys appeared normal macroscopically. The pelvis and ureter on each side were distended with blood clot mixed with whitish material, the epithelial lining showed numerous haemorrhages. Microscopically there was not any crystalline material in the kidney tissue, but the whitish material from the ureters was crystalline and contained 78 per cent of acetylated sulphapyridine. The authors suggest that patients who develop anuria after sulphapyridine have an idiosyncrasy which causes the drug to be excreted in a comparatively insoluble form, deposition of which leads to haemorrhagic pyelitis and ureteritis.

Morbid anatomy and biochemistry

Histological changes

The heart in uraemia.—C. Solomon, I. E. Roberts and J. R. Lisa report on the condition of the heart in fifty patients who died in uraemia. Acute endothelial hyperplasia of the coronary arterioles, producing narrowing or thrombosis, was present in seven of the eight patients who showed renal necrotizing arteriolitis. With the above one exception there were not any cardiac lesions characteristic either of the uraemic state or the associated renal lesions. The kidney lesions were divided into five groups as follows: (1) pyelo-nephritis, eighteen cases; (2) nephrosclerosis, ten cases; (3) necrotizing arteriolitis, eight cases; (4) acute diffuse glomerulo-nephritis, four cases; and (5) chronic diffuse glomerulo-nephritis, nine cases. In a series of forty-nine hearts the weights ranged from 175 to 940 grammes. Acute diffuse fibrinous pericarditis was present in seven cases. Although fibrinous pericarditis is usually considered to be a response to a chemical irritant, it is interesting to note that, in the four cases which were investigated bacteriologically, all showed streptococci. Mild myocardial necroses were present about as frequently as was acute interstitial myocarditis, but acute mild infarctions and other cardiac lesions were seen less often.

Carson, J., and Smith, G. S. (1942) *Lancet*, **2**, 359

Solomon, C., Roberts, J. E., and Lisa, J. R. (1942) *Amer. J. Path.*, **18**, 729.

URETHRA, DISEASES

See also B.E.M.P., Vol. XII, p. 386.

In male**Injuries**

Surgical treatment of rupture of the urethra.—A. H. Hunt and C. N. Morgan report a case of complete rupture of the membranous urethra in a man, aged twenty-four, who was injured by a bus. The patient was admitted to hospital with multiple fractures of the pelvis, with oozing of blood from the meatus and with severe shock. A tender suprapubic swelling developed and a haematoma appeared in the perineum. The man was treated for shock and, when restored, was brought to the operating theatre. The two surgeons on duty simultaneously carried out the following procedures. (1) Through a midline suprapubic incision a pelvic haematoma was evacuated, and a spicule of bone was removed, the bladder was opened and a Liston sound was passed through the prostatic urethra up to the site of the rupture. (2) A large rubber catheter could be passed for a distance of only twenty centimetres into the urethra, being held up at the site of the rupture. A transverse incision was made just behind the urethral bulb and was deepened to expose the tips of the catheter and the sound. The right half of the transverse ligament was divided close to its outer attachment by cutting the ischio-cavernosus and bulbo-cavernosus muscles. The left half had been detached from the pelvis by the initial injury. The triangular ligament, attached only anteriorly, was then swung forward as a flap, and its deep surface was brought into view. (3) The bladder was pressed downwards towards the perineum by one surgeon, which allowed the other surgeon, using the catheter and sound as guides, to approximate the torn ends of the urethra and to suture them together, using an atraumatic needle and fine catgut. Suprapubic drainage was arranged by means of a de Pezzer catheter, and a tube was placed in the cavity of Retzius (preperitoneal space) and a corrugated rubber drain in the perineum. The wounds were then closed. Three pints of blood were given during the operation, and sulphanilamide was administered by mouth for eight days afterwards and was also used for dressing the perineal wound. The result was completely successful, and the fracture united well. The patient was last examined fifteen months after the injury, and he was then well and was doing heavy work; micturition and sexual functions were normal and instrumentation did not show any stricture.

In female**Injury**

Treatment of stress incontinence.—In a paper read before the American Association of Obstetricians, Gynecologists and Abdominal Surgeons V. S. Counseller considers the treatment of acquired urinary incontinence in women. This usually results from injury during childbirth to the internal sphincter, which surrounds the posterior third of the urethra and neck of bladder, to the external sphincter, and to a voluntary muscle, the sphincter membranaceae, surrounding the middle and posterior thirds of the urethra. The last appears to be the most important. An operation designed by Kennedy to restore the sphincter mechanism is described. It consists essentially in plicating the tissues over the urethra and repairing the voluntary sphincter by stitching of the vaginal wall, to which it is intimately adherent. Complete control was restored in twenty-six patients upon whom the author performed the operation. Some patients suffered from cystitis and urethritis after operation but in all cases it yielded readily to treatment.

Counseller, V. S. (1943) *Amer. J. Obstet. Gynec.*, **45**, 479.

Hunt, A. H., and Morgan, C. N. (1942) *Lancet*, **2**, 330.

URINE EXAMINATION

See also B.E.M.P., Vol. XII, p. 393.

Chemical constituents**Lead**

Methods of detection.—W. R. V. Marriott publishes his results of a comparison of various methods for the detection of lead in the urine. A known amount of lead in the form of lead nitrate or lead acetate solution was added to equal volumes of pooled urine. Of the ten methods which were tested spectroscopy seems to be most satisfactory; it is the quickest and is quite accurate. No method is reliable unless the samples of urine are collected directly into lead-free glass containers, such as Pyrex glass. The dithizone methods, such as that of M. K. Horwitz and G. R. Cowgill, and the method of T. V. Lentonoff and J. G. Reinhold are as accurate as the spectroscopic test, but take a longer time, and because of more elaborate procedure it is easier to make an error in them. The modified Fairhall method and the method suggested by D. O. Shiels give results which are too inaccurate to allow any confidence to be placed in their results. There is not any simple or fool-proof way of determining the lead content of urine.

Examination of protein fractions

The anterior pituitary hormone.—G. E. S. Jones and N. L. R. Bucher have devised a method of concentrating and fractionating human urine designed to leave the proteins unchanged. The biological properties of the various fractions have been tested on animals. Large volumes of urine were collected, sulphanilamide powder being added to prevent bacterial growth and

the urine being placed in the refrigerator as soon as possible after collection to avoid destruction of any heat-labile protein. The urine was filtered and then dialysed for about two weeks at 10° C. When the bags became encrusted with salts the residues were combined and placed in fresh bags. The urine was finally dialysed against cold running water to remove the remaining sulphanilamide, urea and salts. Care was taken not to concentrate below one-tenth of the original volume lest the urea content should become high enough to denature the proteins. The final concentrate was filtered by suction with kieselguhr. The hydrogen ion concentration was adjusted to pH 4 by means of the glass electrode and the precipitate was filtered off and set aside. The filtrate was divided into three or five equal parts which were saturated with ammonium sulphate and readjusted to various pH values. The precipitates formed were filtered off. These precipitates were taken up in ammoniated water and saturated again with ammonium sulphate. The pH values were readjusted to their previous readings and the resulting precipitates were again filtered off and kept. This process of purification was repeated from four to six times. The final precipitate was dissolved in a slightly alkaline solution and dialysed against cold running water for twelve hours. The solution was then frozen. The material studied was urine from menopausal women, women below menopausal age and normal men. The test animals were killed after a seven-day course of injections and the organs weighed and examined microscopically. All the specimens tested showed the properties of the follicle-stimulating hormone of the anterior pituitary. This active fraction is best precipitated from a saturated solution of ammonium sulphate at pH 6.8. No evidence of luteinizing hormone, thyrotropic or adrenotropic activity was observed in any fraction of any specimen studied.

Fairhall, L. T. (1922) *J. industr. Hyg.*, **4**, 9.

— (1924) *J. Biol. Chem.*, **60**, 485.

Horwitt, M. K., and Cowgill, G. R. (1937) *J. Biol. Chem.*, **119**, 553.

Jones, G. E. S., and Bucher, N. L. R. (1943) *Endocrinology*, **32**, 46.

Lentonoff, T. V., and Reinhold, J. G. (1940) *Industr. Engng Chem.*, **12**, 280.

Marriott, W. R. V. (1942) *Amer. J. clin. Path.*, **12**, 488.

Shiels, D. O. (1938) *J. industr. Hyg.*, **20**, 581.

UTERUS, DISEASES AND DISORDERS: TUMOURS

See also B.E.M.P., Vol. XII, p. 448; and Cumulative Supplement, Key Nos. 1586–1590.

Fibroid tumours

Aetiology

Incidence in white women and in negroes.—R. Torpin, E. Pund and W. J. Peeples have examined a series of 1,741 cases of fibromyomas of the uterus, in an endeavour to throw some light upon the aetiology. The incidence of such tumours was found to be greater in negro than in white women, the corrected ratio being 3.3 : 1, and the tumours tended to be larger in the former patients. Evidence of pelvic infection (salpingitis) was present in 16.2 per cent of the white women and in 54 per cent of the negroes. Necrosis was more common in negroes, and occurred in 16.2 per cent, as contrasted with 7.8 per cent in white women. It is thought that the greater tendency to fibroids that is present in negro women may be related to their greater liability to keloid scars. The theory that hyperoestrinism is responsible for fibroid growth was not upheld by comparative examination of the endometrium of 100 fibroid and 100 non-fibroid uteruses. Of the former group, in 20 per cent of white women the uterus showed hyperplastic changes whereas in negroes the figure was 10 per cent; in the latter group the percentages were 15 and 20 respectively, that is no special association of endometrial hypertrophy with fibromyomas was observed. Follicular and luteal ovarian cysts were a comparatively common finding, in 19.1 per cent of white women and in 29.3 per cent of negroes.

Morbid anatomy

Mitotic activity in leiomyomas.—P. H. Hartz and M. J. Hugenholtz discuss the significance of mitoses in uterine leiomyomas which, when benign, are usually stated not to show such changes. The authors examined ninety specimens of uterine leiomyomas by a special technique of rapid fixation of the tissues, which is regarded as being responsible for their greater positive findings. Their cases fall into three groups; myomas (1) without mitoses, (2) with few mitoses only and (3) with mitoses which were found easily and in greater numbers. Mitoses were found in fifty-seven, or 63 per cent of the whole group of ninety cases, and in twenty cases, or 22 per cent in group (3). The authors conclude that the occurrence of mitoses in benign leiomyomas of the uterus is quite common, and is not restricted to malignant myomas. The discrepancy between their results and those of other workers can be explained by the difference in histological methods.

Hartz, P. H., and Hugenholtz, M. J. (1942) *Amer. J. clin. Path.*, **12**, 523.

Torpin, R., Pund, E., and Peeples, W. J. (1942) *Amer. J. Obstet. Gynec.*, **44**, 569.

VACCINIA AND VACCINATION

See also B.E.M.P., Vol. XII, p. 515; and Cumulative Supplement, Key No. 1595.

Vaccinia

Lesions in man

Generalized vaccinia (vacciniola).—H. W. Barber records two cases of the rarer form of

generalized vaccinia, namely vaccinal eruptive fever or vacciniola, the other form being generalized vaccinia from auto-inoculation. The first patient was a man, aged fifty-nine, who had the primary lesion of vaccinia on the chin ten years after vaccination; the secondary rash subsided within twenty days of its onset; the incubation between the primary vaccinal lesion and the generalized rash was probably about four days. The second patient was a girl, aged seventeen; the vaccination did not 'take', and the interval between vaccination and the appearance of the generalized eruption was sixteen days. The interval has been variously stated to be from three to fourteen days.

Vaccination

Abnormal results of vaccination

Generalization.—A. A. Jubb of the Ministry of Health reviews the subject of generalized eruption which is recognized as being very rare. Several estimates have been made, from one in every 10,000 vaccinations, one in 100,000 vaccinations and one in 900,000. The figures accepted for the cases during the years 1909–10 to 1941 were 34 among 3,289,733 vaccinations, or one case among 96,756 vaccinations. The concurrence of two such rare conditions as generalized eruption and post-vaccinal encephalitis in the same person must be a very remote chance—one in many millions; only eight cases have been recorded. Generalized eruption in the foetus is also most exceptional; F. W. Lynch recorded a case of pemphigoid eruption in the short-lived child of a woman vaccinated twenty-seven days before delivery; he considered such cases, of which he collected eight examples, one recorded by Edward Jenner, as intra-uterine smallpox. Auto-inoculation (auto-vaccination) is not a generalized reaction, being due to transfer of the virus from the vaccination vesicle to other places on the skin.

Barber, H. W. (1942) *Proc. R. Soc. Med.*, **36**, 43.

Jubb, A. A. (1943) *Brit. med J.*, **1**, 91.

Lynch, F. W. (1932) *Arch. Derm. Syph., Chicago*, **26**, 997.

VEIN DISEASES

See also B.E.M.P., Vol. XII, p. 526; and Cumulative Supplement, Key No. 1596.

Varicose veins

Varicose veins and circulatory efficiency

Report of investigations.—The idea that pooling of blood in varicose veins can reduce circulatory efficiency occurred to E. M. Chapman and E. Asmussen in consequence of seeing a middle-aged woman who complained of attacks of praecordial pain on walking and sometimes on suddenly standing up, although there was not any clinical, radiological or electrocardiographic evidence of heart disease, she had very large varicose veins, however, and was relieved from her symptoms by wearing elastic stockings. With this in mind the authors questioned 250 patients with severe varicose veins and found that forty-seven, or 18 per cent, complained of shortness of breath which was relieved by lying down, and that nineteen of these forty-seven also suffered from mild praecordial pain or palpitation, while three experienced sudden dyspnoea, dizziness and praecordial pain on standing up. None of these patients showed any evidence of organic heart disease, although some had a slightly raised blood pressure. Investigations were then carried out on twelve varicose subjects and seven normal controls. Of the twelve patients, five had the symptoms mentioned: seven returned for investigation after treatment by saphenous ligation and sclerosing injections. The patients were examined in the morning in a fasting state; a tilting table was used, and with the person under examination in the recumbent position, estimations of the basal metabolic rate, vital capacity, pulse rate, blood pressure and arteriovenous oxygen difference were carried out. From the basal oxygen consumption and the arteriovenous oxygen difference the cardiac output was calculated. The patient was then tilted to an angle of 45° and the observations were repeated. In most cases electrocardiograms were taken in both positions. A comparison of the results in the controls and in the patients with varicose veins disclosed the following facts. (1) In the recumbent position the cardiac index, that is cardiac output per square metre of body surface, and stroke volume, that is amount of blood ejected at each systole, were both higher in the varicose veins subjects. The cause of this was thought to be an increase of blood volume, so that in the recumbent position an abnormally large amount returns to the heart. To test this theory the blood volume was estimated and found to average 3.30 litres per square metre of surface as compared with a normal average of 2.93 for males and 2.53 for females. This high value would in itself lay an added burden upon the circulation. (2) In the tilted position the average decline in cardiac output was 5 per cent in the controls and 21 per cent in the varicose veins subjects; in stroke volume, 14 per cent and 39 per cent respectively; in systolic blood pressure, 0.3 per cent and 8 per cent; while the pulse rate showed an average rise of 15 per cent and 25 per cent. After removal of the varicose veins the seven subjects examined experienced relief of symptoms and restoration, partial or complete, of circulatory efficiency. The average increase in pulse rate on tilting in all seven was twice as great before as after ligation. The authors place great reliance on this compensatory increase of pulse rate in measuring the efficiency of the circulatory mechanism.

Injection treatment

Sodium ricinoleate and heparin.—The treatment of varicose veins by a single large dose of

sodium ricineolate is attended by one particular risk, namely the extension of clotting to the deep veins, with the development of oedema of the leg. An attempt to prevent such a complication by using heparin is described by S. H. Sedwitz; the drug does not dissolve a thrombus already formed but prevents further extension of the clotting process. The method adopted is therefore as follows. The patient is directed to report on the day after the sclerosing injection is given; he is then examined for tenderness and discoloration of the skin over and about the veins, for cramp-like pains extending to the groin and lower abdomen and for evidence of impaired circulation, including swelling of the leg. If such signs are found the patient is confined to an oscillating bed and 10,000 units of heparin are given intravenously every four hours. The clotting time is determined before each injection; when it reaches ten or twelve minutes heparin administration is discontinued. In each of fourteen cases all signs of clot extension disappeared and the patient was able to leave hospital within five days. In twenty-nine cases, patients treated without heparin required from two to three weeks' in-patient and from two to three weeks' out-patient treatment.

Modern treatment of varicose veins

Injection and operative methods.—E. Finch describes the modern treatment of varicose veins. The circulation of the leg must first be reviewed as a whole. If the valves are incompetent so that the venous stream is downward when the patient stands, an undue burden is being placed on the deep veins. The latter may be assumed to be patent if oedema of the ankles is not present and if a history is not given of previous 'white leg'. In the absence of occlusion of the deep veins, saphena varix and active thrombophlebitis, treatment by sclerosing injections is satisfactory for mild and moderate varicosities, is ambulatory and has a very low death rate. The solutions most used are 5 per cent sodium morrhuate and 5 per cent monoethanolamine oleate. A dose of 2 or 3 cubic centimetres is given while the vein is full, that is with the patient standing. Care must be taken to avoid injecting fluid outside the vein, which results in necrosis and chronic ulceration. About eight weekly injections are required. The 'spider' type of veins can be injected, but particular care is necessary to insure that the fluid does not escape into the tissues. When the valves in either the superficial or the deep veins or both are incompetent, injection is not enough. Such conditions require ligation and division of the saphenous vein at its junction with the femoral vein and of any branches entering the vein near its termination. This procedure may be combined with injection by passing a fine tube or ureteric catheter down the saphenous vein before the lower ligature is tied and injecting sclerosing fluid while the tube is gradually withdrawn. Excision of portions of the vein is probably justified only when the valves of the communicating or deep veins are incompetent, and should be combined with ligation and division of the saphenous vein.

Varicose veins in the Forces

Most suitable forms of treatment.—The difficulties of treating varicose veins in military patients by injections alone are discussed by E. L. Farquharson. True varicosity is less common in these patients than is a condition of ectasia, which responds poorly to injections, and regular injections are often impossible owing to the continual movements of troops, so that treatment tends to be sporadic and unsuccessful. The Trendelenburg operation has given, in the author's hands, disappointing results even when combined with injections, and in any case necessitates hospital treatment. The method of subcutaneous ligation combined with injection has been used in 150 cases with excellent immediate results. The great majority of patients required only one treatment for each affected limb. About half of them had two ligatures applied, one in the thigh and one at knee level, while the remainder, in whom only the veins below the knee were affected, had one ligature applied at knee level. Most of them returned to full duty within two weeks. Only thirty of the patients could be kept subsequently under observation; in all, when they were examined from two to nine months after treatment, the veins were found contracted to hard slender cords with no sign of re-canalization. The method is not employed in cases in which the dilatation extends right up to the saphenous opening; in these patients open ligation and division is carried out through a small incision without extensive dissection, with injection into the cut lower end before the second ligature is applied. The technique of subcutaneous ligation with injection is as follows. A stitch is passed round the vein at its highest visible or palpable point, and when the latter is in the thigh a second stitch is passed at knee level. Rarely a third ligature is required. The ligatures are most easily applied with the patient standing up. Silkworm gut on a curved cutting needle is employed. The needle pierces the skin about a quarter of an inch on each side of the vein and the stitch is tied over a small roll of gauze. Local anaesthesia is unnecessary. An injection of 20 per cent saline solution is then given into the vein immediately below each ligature. The dose is up to 20 cubic centimetres. Fairly severe cramping pain follows about fifteen seconds after the injection but passes off quickly, as a rule within two minutes. The resulting reaction is usually not severe and the presence of the stitches causes little or no discomfort. If the veins are very much dilated, the patient is detained in hospital for one or two nights, otherwise he is returned to his unit immediately. He is excused all duties for forty-eight hours and is subsequently kept on light duty until the stitches have been removed in a week's time, or, if the reaction has been severe, for a longer period. The limb is kept firmly bandaged for a week to reduce the size of the thrombus. Open ligation of the vein at the saphenous opening is not considered to necessitate removal to hospital provided that it is done through a half-inch incision without any extensive dissection.

Acute superficial thrombophlebitis

Treatment.—W. W. Heyerdale, O. T. Clagett and E. M. Anderson report four cases all seen within two weeks at the Mayo Clinic, in men aged respectively sixty-three, sixty-two, fifty-two and forty-five years, of acute superficial thrombophlebitis in an incompetent venous system of the lower extremities. All the patients had varicose veins. The treatment adopted and recommended entails division and ligation of the greater saphenous vein at the sapheno-femoral junction and injection into the distal segments of a sclerosing solution (such as from 0.5 to 3 cubic centimetres of a 5 per cent solution of sodium morrhuate). In none of the cases were all the veins in the limb involved, nor was there oedema of any degree except in the immediate region of the affected vein. The patient's symptoms were confined to mild fever, dull pain, tenderness, redness and a sensation of stiffness in the part of the extremity affected. Previously in such cases patients were advised to go to bed, to elevate the limb affected and have warm moist applications for days or weeks, treatment of this kind usually results in a prolonged period of disability with an accompanying economic loss. Stress is laid on the conclusion that a patient with acute superficial thrombophlebitis does not need prolonged rest in bed and that rather, even without such rest, he or she can have the offending varicose veins obliterated satisfactorily by a course of treatment very little or no longer than that required for uninvolved varicose veins. High ligation and division of the greater saphenous vein were carried out as soon as possible; the patients were dismissed from the hospital a day or two after ligation, to be readmitted for further sclerosing treatment to eliminate remaining patent varicose veins. The advantages of this treatment are (1) the duration of the acute stage of the disease is shortened, thus redness and tenderness of the affected part rapidly subside, (2) varicosities requiring treatment are obliterated at the same time, (3) there is less possibility of recurrence of phlebitis; and (4) there is less likelihood of pulmonary embolism.

Varicose ulcer

Treatment by blood or plasma A treatment for ischaemic and varicose leg ulcers which has given encouraging results is described by M. Naide. The ulcer is cleaned with peroxide of hydrogen and dried with sterile gauze. Blood (1 to 5 cubic centimetres) is drawn from the patient's antecubital vein and applied by dropping it from the syringe or blowing it from an atomizer on to the surface of the ulcer and spreading it into a film, which is allowed to clot. A dry dressing is then applied. Concentrated plasma may be substituted. Of fifteen refractory ulcers nine healed, two improved and four were unchanged. The theory is that blood or plasma improves nutrition.

EDITORIAL COMMENTARY—Varicose Veins and the Present Era

Attention has again been focused on varicose veins by the mobilization of huge forces of men and women of whom many quite young are found to have incapacity due to this condition.

The first essential is that a correct diagnosis be made, and in order to do this a complete examination of the individual must be carried out to exclude other causes for the symptoms, such as deformities of the foot and diseases of the arterial side of the circulation, for example arteriovenous fistulae of the lower extremity, which may be the result of trauma, although it is usually congenital. In the latter case, however, it often does not become manifest until the second decade of life. Other conditions such as Raynaud's disease and Berger's disease must be excluded. There may also be some obvious cause interfering with the return of blood from the lower extremity, such as an abdominal tumour, disease of the heart, a previous attack of thrombophlebitis (white leg) or any other focus of thrombophlebitis. Before treatment by the injection of sclerosing solutions is decided upon, conditions such as hyperthyroidism, gastro-intestinal disease, diabetes mellitus, renal drainage and allergic manifestations should all be excluded.

Varicose veins are practically confined to the lower extremities and are superficial to the muscular aponeuroses. They are usually apparent in the spare individual, but in the short, stocky or adipose patient they are not obvious and the diagnosis must be confirmed, often with difficulty, by palpation (Schwarz's test). They do occur elsewhere—in the oesophagus, abdominal wall and anal canal, and as varicocele. To define exactly what is meant by a varicose vein is difficult. It is something more than a dilated, tortuous elongated vein with thickened walls. The name should be reserved for those veins which have lost the power to transmit blood to the heart, and this usually implies that the valves are incompetent.

The following questions then arise. (1) Do dilated, tortuous, very obvious veins, but with no demonstrable incompetence in the valves, produce any symptoms at all? (2) Is the patient really merely conscious of the appearance from the purely cosmetic point of view? (3) Do the dilatation and tortuosity appear before the incompetence of the valves arises or vice versa? (4) Can the competence of the valves be preserved by partial obliteration of the lumen—by the injection of sclerosing solutions in the early stages? (5) Can prophylaxis or prevention be secured by change of occupation or by rest? (6) Are the dilated, superficial, obvious, perhaps tortuous, veins really compensatory and are they actually providing a collateral circulation after an attack of thrombophlebitis of the deep veins with consequent obliteration of them? This question indeed involves a very careful examination to estimate the competency of the valves before designating them as varicose and taking steps to obliterate their lumen.

From the point of view of medical officers attached to the Forces, obliteration of any obvious 'varicosity' does remove a cause of symptoms which it is impossible to deny; everyone with

experience of Service cases will agree that the 'varicocele' is always a difficult problem!

Varicose veins which cannot transmit blood back to the heart are absolutely useless—in fact, they are a menace. So far as the lower extremities are concerned—and these are discussed below—the blood actually flows down the veins and so must be returned to the heart by an alternative route. The removal or destruction of varicose veins must aid the circulation and must never be allowed to harm it.

How do the varicose veins rid themselves of their contents? They empty themselves into the deep veins of the leg by the perforating or communicating branches. There are few of these in the thigh, but many below the knee. The communicating veins also have valves which, if competent, allow the blood to flow inwards but never outwards. They are simply the safety vent; the deep veins do the work. If the deep veins are unable, however, to do the work, then the patient complains that the legs feel tired and heavy, the feet are congested and there is swelling of the feet and ankles. This is an easy clinical test to estimate the response of the deep veins, and it is rarely that there is any evidence in a varicose lower extremity that the increased burden is too much for the deep veins. The ability of the latter to deal with this extra load is due to the competence of the valves, the suction action of the thorax and the contraction of the muscles which enclose them, the intermittent action of these enables them to be filled from below upwards. The superficial veins, however, are not enclosed by muscles but embedded in fat between the elastic skin and the aponeurosis.

Many of the aetiological factors are far from clear. Increased intra-abdominal pressure due to laborious work is an important factor. Long continued standing is another, as seen for example in motor tram drivers, and in persons in whom muscular movements of one leg only are necessary—the veins in this leg may not become varicose. Pregnancy is another factor, but the superficial veins may dilate as early as the second month or only in the late months, moreover, they may not appear until after repeated pregnancies.

The annoying, incapacitating, and often extremely painful complications, dermatitis and ulcer formation, are difficult to explain; for example, they never occur in the thigh or foot. Moreover, the rupture of a varicose vein of the lower extremity always takes place between the knee and the ankle; it is often the small inconspicuous vein that ruptures and not the obvious, thin-walled, sacculated one.

The treatment of varicose veins is either non-operative or operative, the latter term including all injection methods. When ulceration has occurred the treatment is governed by the three cardinal factors necessary to obtain healing anywhere in anyone—*rest, improvement of blood supply and the prevention of infection*. The more thorough the application of these principles the sooner healing occurs. It was cynically said of the chronic varicose ulcer that the best way to get it to heal was to break the femur. The non-operative treatment by bandages and stockings will answer in some cases, and the ambulatory treatment of ulcers can be carried out by employing pressure with a rubber sponge over the ulcer (McPheeter's 'venous heart') or by rest, splinting with Unna's paste, elastoplast, or plaster of Paris.

Injection of sclerosing fluid was introduced by Pravaz in 1851 and again popularized by Linser of Tübingen in 1911. Since then sclerosing solutions have been used quite indiscriminately often with no attention to aetiological, anatomical, physiological or pathological conceptions of the condition. The consequence has been that many failures have occurred, and an excellent method of treatment has often fallen into disrepute. It is particularly ineffective when there are leaking communicating veins ('Trendelenburg double').

The inherent disadvantages of any injection treatment are as follows. (1) A 'wandering' obstinate thrombophlebitis may occur. (2) Recurrences are common and may be very diffuse and difficult to treat. (3) Occasionally an injection ulcer may occur owing to the sclerosing fluid getting into the tissues surrounding the veins. (4) Pulmonary embolism, which fortunately is extremely rare, may be set up. (5) The patient may react 'allergically' to the sclerosing fluid employed. The first two can be avoided by resection of the saphenous vein at the sapheno-femoral angle, and the last by testing the solution to be used by injecting a small dose at least twenty-four hours before giving the actual treatment.

The four cardinal sins of chemotherapy (V. E. Lloyd, 1941) also apply to the injection treatment of varicose veins: (1) to expect too much from the drug; (2) to promise too much to the patient; (3) to be easily satisfied with the early response; (4) to neglect tests of cure.

Many different sclerosing solutions have been used: 5 per cent sodium morrhuate, 5 per cent sodium oleate, 50 per cent dextrose, 30 per cent sodium salicylate, 10–20 per cent sodium chloride, and quinine hydrochloride 0.26 grammic (4 grains) and urethane 0.13 grammic (2 grains) provided in ampoules containing 2 cubic centimetres of solution in distilled water. The solution most commonly used is 5 per cent sodium morrhuate, 2–7 cubic centimetres being the dose.

The indications for simple injection treatment are (1) varicose ulcer which is 'riding' on a vein, the connexion between which and the ulcer is clearly visible; (2) obliteration of an unsightly but otherwise symptomless varix. The methods employed by different authorities have only one thing in common, namely that the solution must be injected into the lumen of the vessel. Some inject into the vein when it is distended, others when it is empty; some inject when the patient is standing, others when he is lying down; some begin above the knee, others below; the injected fluid probably reaches a point below the knee if the vein is distended as the blood is flowing downwards. Some give one injection at a time, others inject

into several places at the same 'sitting'; some space the interval between the injections to seven days, others give a daily injection; some try to limit the area under the influence of the injected fluid by the use of lightly applied tourniquets, others think this unnecessary; some apply pressure immediately to the site of injection or keep it elevated for twenty-four hours at least, others regard this as useless. And some say that the patient should walk about immediately after the injection in order to promote the flow of blood from the limb; but on the other hand, rest with the limb elevated for twenty-four hours will drain the blood away more efficiently. It can only be repeated that whatever the technique may be, the sclerosing fluid must be injected into the lumen of the vein as shown by the extraction of blood into the syringe before making the injection.

Whatever may be the treatment, in any case and at all ages when there are incompetent valves in the superficial veins, the long saphenous vein must be resected at the sapheno-femoral angle. No branch must be left undivided so that it opens into the proximal stump of a varicose long saphenous vein. The operation can be done under a local anaesthetic but the equipment of a good operating theatre is essential. It is often a very tedious operation in the adipose, and may be very difficult, even dangerous, when the proximity to the femoral vein and the thinness or friability of the terminal portion of the saphenous vein are remembered (L. K. Stalker and W. W. Heyerdale, 1939). It is generally agreed that the mere ligaturing of the long saphenous vein somewhere near its termination, or a blind procedure such as passing a ligature on a needle beneath it and tying without making an open dissection, is doomed to failure by recurrence, although at first the method may appear successful. There is often an accessory long saphenous vein, and dealing with this alone is worse than useless. High ligature should be combined with retrograde injection into the distal portion of the vein. The secondary thrombosis in the calf which so often occurs after this procedure can be avoided by combining the high resection with resection also at the level of the knee. Any varices left unobliterated by this procedure can be dealt with by local injection later.

The results of the tests will indicate whether the external saphenous vein is to be treated by resection and retrograde injection in the same way. Operative resection (excision) of varicose veins has a definite place in the treatment. The indications are as follows. (1) Especially large veins in the young or middle aged (2) Persistence of the varicose ulcer after successful obliteration of the visible connecting vein; such persistence is probably due to a leaking communicating vein beneath the ulcer, and this should be excised. (3) Proof that leaking communicating veins due to incompetent valves are a factor in production of the varix.

- FRNEST FINCH

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VELDT SORE

See also B.E.M.P., Vol. XII, p. 538.

Clinical picture and complications

Incidence among fair-haired persons

Exposure to sunlight is suggested by J. M. Henderson to be the chief factor in the development of desert sores. A number of such cases occurred in the desert armies during July and August, 1942 and the author has studied a series of fifty patients, each with not less than six lesions. The initial lesion is a vesicle from 2 to 19 millimetres in diameter which develops without itching or pain and is frequently multiple. There is no surrounding infiltration or redness of the skin. The author inoculated himself with the fluid from one of these vesicles without result, so that it is unlikely that a virulent organism is present. Twelve to twenty-four hours after the vesicle forms, rupture and suppuration take place and the lesion increases in size, spreading in the subepithelial plane. Twenty-nine of the patients gave a history of knocks or cuts but in only six had injury occurred at the site of every sore. Facial impetigo was present in twelve cases, an incidence high enough to suggest that the relation was not fortuitous. The sores occurred mainly during the hottest weather and only in exposed areas of skin, most often in people who were sensitive to sunlight and did not tan well. Of the patients with desert sores 70 per cent were fair-haired and 76 per cent blue-eyed; in a control group, the respective percentages were 36 and 28. The skin of people who show a deficient pigmentation reaction to sunlight tends to be abraded by the least knock. The liability of the hands to trauma may partly explain the predilection of desert sores for that region. They proved very resistant to treatment. The wearing of sleeves and long trousers and the use of oil or cream on the hands are advised as prophylactic measures.

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VERTIGO

See also B.E.M.P., Vol. XII, p. 544.

Labyrinthine or aural vertigo*Aural vertigo without suppuration*

Ménière's syndrome.—In an address to the New York Academy of Medicine M. Atkinson emphasized the point that in any case of Ménière's syndrome it is essential first to rule out organic disease of the central nervous system, for example a tumour of the cerebellopontine angle, or of the aural apparatus, such as a stricture of the pharyngeal (Eustachian) tube; and secondly to determine whether the case should be classed as allergic or non-allergic. The latter point can be settled by means of the histamine test, performed as follows: 0.01 milligram of histamine dihydrochloride is injected intradermally, in the normal person a wheal with a white centre appears immediately. In five minutes this has changed to a yellowish wheal from $\frac{1}{2}$ to $\frac{1}{2}$ inch in diameter surrounded by a flare of erythema from $1\frac{1}{4}$ to $1\frac{1}{2}$ inches wide. The wheal begins to fade in ten minutes, and in twenty minutes has vanished. In sensitive people the wheal is larger (from $\frac{1}{2}$ to $\frac{3}{4}$ inch in diameter) and the flare is wider (from 2 to $2\frac{1}{2}$ inches) and shows one or more trailing 'processes' an inch or more in length. The reaction does not begin to fade for fifteen or twenty minutes. Intermediate appearances are sometimes seen and if the reaction is doubtful the test should be repeated in forty-eight hours with double the dose of histamine. Unless an unmistakable 'pseudopod' then develops the result should be regarded as negative. Of 108 patients tested twenty were histamine-sensitive. It is believed that the basis of the attacks in such people is a process of vasodilatation. In the much larger histamine-insensitive group the underlying process is believed to be one of vasoconstriction. At all events the administration of vasoconstrictor drugs to patients in this group precipitated an attack of vertigo whereas the administration of vasodilator drugs has relieved them. Histamine-sensitive patients were treated by gradual desensitization to histamine. Histamine-insensitive patients were given nicotinic acid, a vasodilator, orally and by injection. The optimum dose was found by trial. Complete relief was obtained by twelve of fourteen histamine-sensitive patients and by twenty of forty-nine histamine-insensitive patients.

Deafness and Ménière's disease

Persistence of tinnitus after operation. C. I. Johnson defines Ménière's disease as a disorder of the peripheral vestibulo-cochlear apparatus to be distinguished from vertigo due to lesions of the middle ear or brain, or associated with other diseases. The symptoms are disturbance of gait and posture, with a tendency to stagger and fall, disturbance of limb motion; nystagmus or ocular deviations, vertigo, vague phenomena such as pallor, sweating, nausea, vomiting and fainting, and disturbances of hearing (deafness, tinnitus). The syndrome implies changing function of one of the labyrinths, and disappears when that labyrinth is completely out of action. The attacks are intermittent and are usually sudden and incapacitating. Nystagmus is usually present during the attack, in most cases towards the normal labyrinth. It is a useful diagnostic sign. Deafness always occurs sooner or later. It is of the inner ear or perception type and is progressive. The patient may be unaware of the deafness, which is discovered by audiometry. Tinnitus is of value as a localizing sign when it increases in one ear during the attack. The differential diagnosis is of great importance. Middle ear disease must be excluded; when this has been done audiometry is the next step, and will invariably show some degree of perception deafness. The Bárány tests usually show a percentage loss of activity corresponding roughly to the percentage loss of hearing. The responses are normal in kind but are diminished in degree and are delayed. The severe forms of Ménière's syndrome are rarely encountered. In the milder forms treatment with potassium chloride sometimes gives an excellent result. Furstenberg believes that reduction of sodium in the body will stop the attacks. He advocates a salt-free diet together with large doses of ammonium chloride. In the more severe cases section of the eighth nerve may be undertaken. The author reports three cases in which this was done with good results. Tinnitus sometimes persists even after nerve section, a phenomenon which may be likened to the sensations referred to an amputated extremity. In some cases the syndrome appears to be of allergic origin. Of twenty-two patients on whom a histamine test was done eight reacted positively and were successfully treated by desensitization. Histamine therapy sometimes gives good results. The fact that spontaneous remissions may occur render it difficult to assess the results of treatment. In one large series, such remissions, lasting from a few months up to twelve years, were noted in 41 per cent of the cases.

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VITAMINS

See also B.E.M.P., Vol. XII, p. 570; and Cumulative Supplement, Key Nos. 1601-1609.

Other vitamins*Vitamin K*

Hypovitaminosis K in anorexia nervosa.—A case of vitamin K deficiency in a woman, aged thirty-two, with anorexia nervosa is reported by P. M. Aggeler, S. P. Lucia and H. M. Fishbon. The patient had suffered from anorexia nervosa for five years, and had lived on a semi-starvation diet. She had noticed ecchymoses five days previously and had had gingival bleeding for one day. She showed a generalized purpuric eruption, severe hypoprothrombin-

aemia and a greatly prolonged clotting time. Synthetic vitamin K was given intravenously and by mouth. Bleeding ceased immediately, the prothrombin concentration and the clotting time returned to normal and the ecchymoses disappeared within a week. Oddly, there were not observed any signs of deficiency of other vitamins.

Dietetics and applications

Use of vitamins in ophthalmology

The main effects of vitamins on the eye—A paper read by A. J. Baer before the Kansas City Society of Ophthalmology and Otolaryngology deals with the vitamins in ophthalmology. The subject of vitamins is one of which in spite of much research work little is yet known. New ones are constantly being discovered and it is believed that their functions are inter-related so that deficiency or excess of one may be followed by impaired activity of another. Typical cases of vitamin deficiency are rare but hypovitaminosis complicating other diseases is relatively common (1) The importance of vitamin A in ophthalmology was first recognized in 1917 when Dutch children fed on margarine developed xerophthalmia, nevertheless as early as 1500 B.C. it was known that night blindness could be cured by giving liver. Vitamin A is a component or precursor of visual purple. The chief ocular manifestations of vitamin A deficiency are, in order of their appearance, night blindness, xerosis of the conjunctiva, loss of lustre and wrinkling of the conjunctiva with Bitot's spots, xerosis of the cornea and true keratomalacia. (2) The vitamin B complex includes at least seven factors of which two are known to influence the eye. Vitamin B₁ (thiamin) deficiency is believed to be responsible for the amblyopia of chronic alcoholism. Good results have been reported from the use of thiamin chloride in herpetic keratitis. Ocular changes believed to be due to vitamin B₂ (riboflavin) deficiency are burning of the lids, mild photophobia and keratitis. Evidence is conflicting concerning the influence of the vitamin B complex on cataract formation. (3) The cataractous lens has been shown to contain greatly diminished amounts of vitamin C, but that this may be the result rather than the cause of cataract is suggested by the fact that opacities fail to clear up when vitamin C is administered. (4) Vitamin D deficiency has been thought to play a part in the aetiology of myopia. A low blood calcium has been found in myopic individuals and improvement has been claimed to follow administration of vitamin D both in myopia and in keratoconus. (5) Vitamin K deficiency may have some bearing on retinal haemorrhage, of which one case is reported to have improved on vitamin K therapy.

Haemostasis

The effects of different vitamins on haemostasis—In a Honyman Gillespie lecture, H. Scarborough deals with the part played by vitamins in the control of bleeding. The factors operating in haemostasis are coagulation time, clot retraction, bleeding time, capillary resistance, intravascular pressure and what may be called the thrombocytone, that is the number and functional efficiency of the thrombocytes in the blood. Vitamin deficiency may influence any one of the above factors. In idiopathic purpura reports suggest that about one-third of the patients are favourably influenced by vitamin C administration, others by vitamin A. Fifteen patients treated by the author with vitamins C, A and P were not benefited. In obstructive jaundice vitamin K checks the haemorrhagic tendency, provided that hepatic function is adequate. Vitamin K has also proved valuable in certain cases of haemorrhagic diathesis of the new born. Vitamin D has been found beneficial in obstructive jaundice. As regards scurvy, the author has been unable to show that ascorbic acid has any effect, vitamin P, however, is capable of raising a low capillary resistance, and experimental deprivation of this vitamin has produced petechial bleeding with low capillary resistance in two subjects. The author concludes that two forms of bleeding may result from hypovitaminosis, one form being due to deficiency of vitamin C, the other to vitamin P deficiency.

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VULVA AND VAGINA DISEASES

See also B.I.M.P., Vol. XII, p. 606.

Vagina

Vaginitis

Vulvovagino-cervicitis due to chrysotherapy—D. N. Barrows and E. T. R. Stone, in reporting a case, say that they do not find any previous record in medical writings in English of a vulvovagino-cervical eruption being caused by the intravenous administration of gold sodium thiosulphate. The authors' patient, aged thirty-seven, was admitted to an arthritis clinic for gold treatment. Gynaecological examination at that time did not reveal any abnormality of the genitalia. The woman received increasing doses of gold sodium thiosulphate, amounting to a total of 290 milligrams, for a period of three months, at the end of which time oral lesions developed and treatment was discontinued. Two weeks later a generalized rash appeared, and six weeks afterwards the patient again attended the clinic. Examination then showed a macular rash on the vulva, vaginal walls and cervix. Biopsy of the affected skin showed collections of a golden yellow substance, which was probably gold, in the dermis. It

is suggested that a purpuric condition of the endometrium may account for the uterine haemorrhage which is sometimes observed in patients during chrysotherapy.

Observations on trichomoniasis.—R. E. Trussell and Mary E. Wilson have investigated three aspects of vaginal trichomoniasis, as follows. (1) *Serological reactions.* To estimate the value of the complement fixation test, the results which were obtained in 400 pregnant women were compared with the results of 'hanging drop' investigations and with cultural methods of diagnosis. Of the 400 women, trichomoniasis had been diagnosed in 110 by the two last-named methods. The percentage of the 110 subjects who gave a positive complement fixation test was 47.27 whereas, of 290 in whom trichomonas had not been found by either method of examination, the percentage of positive reactors was 16.55. Positive reactions were commoner in patients with vaginitis than in carriers. The authors conclude that examination of fresh vaginal discharge is the easiest method of diagnosis and is sufficiently reliable for practical purposes. Culture occasionally demonstrates the organism in a case in which direct examination is negative. The complement fixation test is not worth doing. (2) *Puerperal morbidity.* The study of 880 newly delivered women did not lend any support to the view that trichomonas is a source of danger during the puerperium. The respective percentages of cases of one-day fever and of puerperal morbidity (the temperature reaching 100.4° F. or more during at least two days) were as follows: women with trichomonas, 14.3 and 8.5; women without trichomonas, 11.7 and 8.3. (3) *Transmission to babies.* Forty-one female babies who were borne by infected mothers were examined during the first eight days of life. Hanging drop preparations were taken from the vagina and from the introitus, and in most cases two examinations were made; two of the infants (4.8 per cent) were found to be infected at the second examination. Risk of infection of the baby therefore exists, but is not great. The duration of the infection was unknown, because the cases were not observed subsequently.

Treatment—At a meeting of the Chicago Gynecological Society E. Allen and H. C. Baum presented the results of treatment of vaginitis in 282 patients. Complete examination was first carried out, including determination of the hydrogen ion concentration of the discharge and microscopical examination of wet and stained smears. In doubtful cases cultures were made. The vaginal discharge showed trichomonas in 166 cases, trichomonas and monilia in sixteen, monilia alone in sixty and non-specific infections in forty. Catheter specimens of urine from 160 patients were examined; trichomonas infection was found in thirty-eight, streptococcal or colon bacillus infection in sixty-one. Trichomonas infection of the bladder is most likely to be detected when the last few drops only of the residual urine are examined. Cystoscopy in such cases usually showed infection and sometimes petechial haemorrhages around the bladder neck. Patients showing changes in the bladder generally had an abnormally patulous urethra; in some cases it was almost funnel shaped. Treatment of the associated urinary tract infection can materially improve the results of treatment of the vaginitis itself, and the authors emphasize the importance of not neglecting this aspect of the case. In treatment they find that instillation of an acid jelly gives the best results. A 'basic jelly' is used of which the pH is adjusted to 4.5 with acetic acid. The addition of various chemicals (gentian violet, certain sulphonamides, iodine) did not appreciably influence the results. No untoward results of treatment with acid jelly were noted and it is considered a safe method for use during pregnancy. Of the 282 patients 115 were considered cured, that is they showed three consecutive negative smears, and 239 became symptom free. Reinfection may take place from the internal genital organs, bladder or rectum. The authors plead for more thorough examination, and for closer cooperation between the gynaecologist and the genito-urinary surgeon.

Treatment by oestrogen—W. E. Brown has studied the results of treating vulvovaginitis in young girls by oestrogenic substances. The theoretical basis for this treatment is the observation that the vulvovaginitis usually subsides when cornification of the vagina occurs at the establishment of puberty. The present group of patients included thirteen with gonorrhoeal infections and six with non-gonorrhoeal infections. In each of the cases one or other of the sulphonamide preparations had been tried previously without success. All of the patients were cured by oestrogen therapy, and the author believes that if vaginal cornification, which can be confirmed by periodic vaginal smears, is maintained for four weeks the percentage of failures will be small. No recommendation is made as to dosage, because it is felt that each patient presents a separate problem; large doses were the rule. Complications were not observed. If the oestrogen is given in a suppository, care must be taken that the patient is not sensitive to the vehicle employed. Gonococcal urethritis is not curable by oestrogenic substances.

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WHOOPING-COUGH

See also B.E.M.P., Vol. XII. p. 616; and Cumulative Supplement, Key No. 1613.

Bacteriology and morbid anatomy

Bacteriological studies

Variant phases of Haemophilus pertussis.—E. W. Florsdorf and A. C. McGuinness describe

the results of studies of *Haemophilus pertussis*. Immunologically this organism is of a single type, but it tends to undergo dissociation into three variant forms which are indistinguishable morphologically from the parent form. On the basis of the serological properties of the variant forms *H. pertussis* can be classified into four 'phases'. Phase I is represented by the virulent form freshly isolated from patients with active whooping-cough. The only means of determining the phase of the organism is by serological surface tests such as agglutination or phagocytosis, using the appropriate antisera. Phase I antiserum will react with phase III organisms; phase III antiserum will not react with phase I organisms. Hence both sera must be used in order to establish that a given organism is in phase I. Phase IV organisms are less readily mistaken, because phase I antiserum does not react with them. Phase II organisms are rarely encountered. Two toxins are present in all phases; one is thermostable, the other is extremely thermolabile, the latter possessing the greater potency. The toxins are not antigenic in human beings to a degree sufficient to produce demonstrable amounts of antitoxin in the serum of convalescent or artificially immunized persons. Serum from adult donors immunized by phase I vaccine has, nevertheless, proved very effective in prophylaxis and treatment. In rabbits a small amount of antitoxin can be demonstrated after injection of living organisms or of their extracts. The non-virulent variant phases contain the same toxins, but only about one-tenth of the amount present in phase I. For the preparation of effective vaccines it is essential that phase I organisms should be used. Another micro-organism, *Bacillus parapertussis*, has been described as the cause of a mild form of whooping-cough. A common minor antigen is present both in this organism and in *H. pertussis*. Cross protection is apparently seldom observed. The toxins of *B. parapertussis*, however, are immunologically the same as those of *H. pertussis* but are present in only about one-tenth of the quantity contained in *H. pertussis* phase I. Cutaneous tests for susceptibility and for final diagnosis in whooping-cough have so far proved unreliable because the reagents used have contained both agglutinin and toxin. The former causes a reaction in immune people, the latter in susceptible people. The authors have prepared agglutinin free from toxin and toxin free from agglutinin, and therefore the two can now be tested separately.

Complications and sequelae

Central nervous system changes

Brain lesions and psychopathic disturbances—L. A. Lurie and S. Levy have studied the effects of an attack of whooping-cough in early infancy upon the personality and behaviour of the child. Of a series of 500 problem children who had been treated at a child guidance home, the number with a history of whooping-cough was 243 (48.6 per cent). In fifty-eight the attack had occurred at or below the age of two years, in sixty between two and five and in forty-one above the age of five. In eighty-four the date of the illness could not be ascertained, the history merely stating that it occurred in early childhood. The fifty-eight children who had had whooping-cough at or below two years of age furnished the material for study. Of these children thirty-four (58.6 per cent) were considered to have suffered some structural changes in the brain during the attack of whooping-cough; this group consisted of twenty-four boys and ten girls. The ages at which they were referred to the child guidance home ranged from four years and four months to seventeen years and four months. Twenty-one were children referred for general behaviour problems including delinquency and various psychopathic manifestations, eight on account of school maladjustment and five for 'general nervousness'. None of the children had suffered from any infection or from head injury prior to the attack of whooping-cough. Sixteen children were stated to have been late in walking or in talking after the attack. Two children who had begun to walk and talk before having whooping-cough had ceased to do so for lengthy periods afterwards. Nine children had had convulsions during the illness and in one they continued to occur up to the time of admission to the home. The general physical findings and the blood Wassermann and Kahn reactions were negative in all the children, and the tuberculin reaction was negative in all but one. Nine showed various endocrine disturbances. Positive neurological findings were present in twenty-five; the signs pointed to a pyramidal lesion in thirteen, to an extrapyramidal lesion in two, and to a combination of both lesions in ten cases. Nerve deafness was a particularly common symptom, occurring in fifteen children. Nine had speech disorders of various kinds. Electroencephalograms were obtained in six cases, and in five they were abnormal. On the basis of the tracings the diagnosis of epilepsy was made in two children, of general cerebral dysrhythmia in two, and of cortical deterioration in one. The results of psychometric tests were: superior intelligence, two children; average intelligence, eight; subnormal intelligence, nine; borderline, five; feeble-minded, ten. Classified according to behaviour the children were divided into four groups as follows. (1) Pre-psychotic and psychotic, with emotional poverty an outstanding feature, eight cases; (2) progressive intellectual deterioration, six cases; (3) post-encephalitic with hyperactivity, destructiveness and so forth, seventeen cases; (4) mixed, showing characteristics of two or more of the foregoing groups, three cases. The authors accept the view that the changes in the brain are probably not, except possibly in rare instances, of an encephalitic character, but are most likely of circulatory origin.

Diagnosis and differential diagnosis

Diagnostic methods

Nasopharyngeal cultures and cough plate cultures.—The value of the nasopharyngeal culture method of diagnosis of pertussis is confirmed by Anne M. Brooks, W. L. Bradford and G. P.

Berry. The swab for taking the cultures was prepared by wrapping a small piece of cotton-wool about the end of a 6½-inch length of flexible wire. The swab was placed in a test-tube and was autoclaved. The culture was taken by passing the swab back through the patient's nostril until it touched the posterior pharyngeal wall; it was taken from one side only. With a little experience the procedure was carried out rapidly and entailed practically no discomfort to the patient. The culture was made on Bordet's medium and was incubated for seventy-two hours. For comparison 198 cough plate cultures were made from 157 patients. Of the nasopharyngeal cultures 438 were made from 248 patients. Positive results were obtained from 52 per cent of the nasopharyngeal and from 37 per cent of the cough plate cultures. When 183 simultaneous cultures were made by the two methods in 165 cases of pertussis, 57 per cent gave positive results by the nasopharyngeal culture method and 34 per cent were positive by the cough plate method. In infants under three the respective percentage figures were 57 and 25.

Treatment

Preventive

Intradermal tests.—Harriet M. Felton and F. W. Flosdorf present the results of intradermal tests for susceptibility to whooping-cough by means of a purified agglutinin of phase 1 *H. pertussis*. Of 776 children tested, ninety-four babies without any history of whooping-cough or vaccination against it reacted negatively, that is they were all susceptible. Of 305 children who had been immunized previously twenty-three, who had received vaccine of doubtful potency, showed negative reactions, 112 were weakly positive and 170 positive. Of 113 children with a history of whooping-cough twenty-one gave a negative, thirty-eight a weakly positive and fifty-two a positive response. In 264 cases the history was unknown; a negative reaction occurred in sixty-one, a weakly positive reaction in eighty-five and a positive reaction in 118. The authors are satisfied with the accuracy of the test in predicting sensitivity and furthermore find that it increases any pre-existing immunity.

Curative treatment

Effects of altitude and low atmospheric pressures.—The claims made for the method of treatment by which patients with whooping-cough are taken up in aeroplanes have been tested by two members of the Berne School Medical Service. Their results are summarized in an Annotation in the *British Medical Journal*. The patients were mostly school children, but included some toddlers and infants and a few adults. Each flight lasted about ninety minutes, of which about forty were spent at heights of from 11,000 to 12,000 feet. Rapid ascent to a great height was ruled out as dangerous. The flights usually took place in the mornings, and observations on weather and humidity were included in the records. Only a few children were apprehensive before going up and none minded when once he was in the air. The younger patients usually slept from the time they reached the height of about 6,000 feet until the time of landing. The only disturbance caused by the flights was nausea, which was experienced by about 30 per cent of the children and adults. None of the infants vomited. The authors collected 250 cases, all in the paroxysmal stage of whooping-cough. In fifty-seven (22.8 per cent) an abrupt cure took place within three days, and often immediately, after the first flight. Another eighty (32 per cent) were 'cured' more slowly, a period of eight days being required. Thus some therapeutic effect of the flights was apparent in 55 per cent of the cases, a further 411 patients were improved. In sixty-nine cases change was not observed, two of the last group were taken up a second time with good effect. Two further series of observations were made, one on the Jungfrau and one in low-pressure chambers. Results of the former experiments were disappointing. With low-pressure chambers only 19 per cent of the patients failed to improve.

Prophylaxis and treatment

Active and passive immunization in children.—J. G. M. Bullowa and Janet Alterman have studied the possibilities of active and passive immunization in the prophylaxis and treatment of whooping-cough. Active immunization was practised upon 135 children. One hundred were given injections of pertussis toxoid antigen, thirty-five were given injections of pertussis vaccine; none of the children had been previously immunized. The toxoid was prepared by adding formaldehyde to pertussis toxin, and it contained 300 units of toxin per cubic centimetre. Each child received 2 cubic centimetres once a week for four weeks. Samples of venous blood were taken beforehand and at one and six months afterwards. Both toxoid and vaccine produced a rise in blood antitoxin content in 75 per cent of the patients. An attempt was made to modify the course of the disease by giving toxoid or vaccine; of eleven children receiving vaccine injections nine had a rise of antitoxin titre but the course of the disease showed little change. Thirty-three children received toxoid or antigen; in four a rise of titre was observed, but clinical improvement did not take place. Passive immunization by antitoxin was attempted in thirty-three children with pertussis and prophylactically in twenty-five children exposed to the infection. Only one of the latter contracted the disease; in the former group no effect was noted.

Intranasal immunization

Experimental results in mice.—Experimental work on the active immunization of mice against pertussis by the intranasal route is described by E. A. North and G. Anderson. The criteria of immunity were reduction in mortality or delay of death in mice intranasally infected with a lethal dose of living *H. pertussis*, and prevention of lung infection in mice given a

non-lethal dose. The results showed that in mice immunized by the intranasal route a much higher degree of immunity developed than in animals immunized by the intraperitoneal route. A high degree of immunity persisted at least into the fifth week, as compared with a duration of about four weeks of immunity in the intraperitoneally immunized group. Multiple intranasal injections were found to bestow a higher degree of protection than did a single injection. To determine the respective degrees of immunity acquired by intranasally and intraperitoneally immunized animals, three groups of fifty mice were taken. The first group was immunized intranasally, the second was immunized intraperitoneally, with a single dose of phase I pertussis vaccine. The third group was left untreated to serve as a control. Three weeks later fifteen mice were taken from each group and were inoculated with a large dose of *H. pertussis*. The survivors numbered fifteen from group 1, nine from group 2 and three from group 3. The immunity produced by intranasal inoculations is considered to be partly general and partly local. Serum from groups of mice inoculated respectively by the intranasal and the intraperitoneal routes did not show any significant difference of potency when used to produce passive immunity in other animals. Hence the higher degree of immunity observed after intranasal injections is probably due to a local factor which appears to be non-specific, developing also after injection of vaccines prepared from various organisms related antigenically to *H. pertussis*.

EDITORIAL COMMENTARY—Clinical Aspects of Whooping-Cough

All modern investigations favour the view that *H. pertussis* is the causal organism of whooping-cough. It grows in the mucous membrane of the upper respiratory passages, trachea and bronchi, surrounding itself with mucus, which protects it from phagocytosis. The expiratory spasmodic cough is a protective mechanism developed by the body to rid itself of this mucus. The inspiratory whoop through a narrow glottis is most characteristic in young children, but it is commonly absent in infants under three months, in children over five years, in adults and in the modified form of the disease which may occur in immunized children. The disease was made notifiable in October, 1939. In 1941, a year of fairly high prevalence, 173,331 cases were notified in England and Wales and there were 2,383 deaths, a figure approximating to the diphtheria deaths for the same year. The most serious complications are broncho-pneumonia and convulsions, both of which have a tendency to appear as late as the third or fourth week of the disease, and are often accompanied by patchy collapse of the lungs. The pneumonia may sometimes be associated with sulphonamide-resistant organisms, such as *H. pertussis* itself, *H. Pfeiffer* and so forth—a point difficult to prove. This pneumonia is certainly more resistant to sulphonamide treatment than is the broncho-pneumonia of measles. Convulsions are of complex origin but are probably most often the result of brain damage due to anoxaemia and tissue anoxia or to oedema. Oedema, cellular degeneration, minute haemorrhages and lymphocytic plugs in the arterioles of the brain have been described. If recovery from the above complications is not prompt, serious sequelae may arise in later life—bronchiectasis and pulmonary damage from the broncho-pneumonia, and behaviour disorders, which may be of the post-encephalitic type, from the convulsions. In practically all severe cases of whooping-cough X-ray films show lung shadows somewhat similar to the shadows of pneumonia. In infants under three months old the mortality from whooping-cough is very high and everything practicable should be done to protect such infants from this infection.

As regards diagnosis the results of laboratory investigations are, on the whole, disappointing. The cough plate, a 50 per cent blood agar plate held a few inches in front of the patient's mouth during a spasm, is not reliable for routine diagnosis although, under special conditions, it may yield a high percentage of positive results in the first week or two of the disease. A thin nasal swab passed along the floor of the nose to the pharynx has recently been reported to yield better results. A lymphocytosis of over 55 per cent is usually present during the first week and, if combined with suggestive cough, is practically diagnostic.

The hope of the future in the prophylaxis of whooping-cough, as in that of diphtheria, lies in universal active immunization of children. It is essential to use an active vaccine made from phase I organisms recently isolated and not frequently subcultured. This vaccine is the only immunizing agent which can be relied upon to produce the antibacterial antibodies which are essential to immunity. Antitoxins, which may be produced in greater quantity by various pertussis toxin extracts, are not fully effective immunizers. The best immunization programme is now believed to be the combination of pertussis phase I vaccine with diphtheria alum precipitated toxoid (A.P.T.) in two doses at one month's interval in children from nine to twelve months old. I. H. Maclean (1940), I. H. Maclean and C. Evans (1941), and J. A. Bell (1941) have demonstrated the value of the long interval of one month between doses. A total dosage of from 12,000 to 20,000 million *H. pertussis* may thus be effective in place of the larger doses formerly employed. A third dose of whooping-cough vaccine should be given a week or two after the second combined injection. Later an additional dose of vaccine should be given at any time when the child is exposed to infection, and in any case when he enters school, in order to reinforce his immunity. Whooping-cough vaccine may be given independently of alum precipitated toxoid and to children of any age, even during an epidemic. Under the age of six months, unfortunately, there is a very poor antibody response. Reactions to immunization are negligible in young children, but are more severe in older children and

in adults. Immunity resulting from the vaccine can hardly be expected to be absolute, but attacks of whooping-cough in immunized children are relatively uncommon, are generally mild and clinically may be almost unrecognizable. Infectivity from the modified attacks is also greatly reduced.

Treatment is relatively unsatisfactory, hence the emphasis on the importance of prophylaxis. New-born infants should never be exposed to the infection. Any patient with the disease in the house should be removed to hospital or elsewhere before the infant appears. If this is not possible the infant should be kept covered with muslin and should be given from 10 to 20 cubic centimetres of convalescent serum at three-weekly intervals. A child with whooping-cough need not be kept in bed but should be protected from cold winds. Antispasmodics and sedatives such as belladonna and phenobarbitone have a very limited place in therapeutics and are not for routine use in young children. Vitamin C and ultra-violet light have had their advocates, but claims that their use reduces the spasms have not been substantiated. They may, however, be useful as general measures. Pure pertussis vaccines are useless in treatment except possibly in the catarrhal or pre-whoop stage. There is, however, some evidence that mixed vaccines containing *H. Pfeiffer* and *H. pneumococcus*, given at three-day intervals during the course of the disease may reduce the incidence of broncho-pneumonia. Sulphonamide prophylaxis of complications is difficult to apply since broncho-pneumonia and otitis media often develop as late as the fourth week. Sulphathiazole, the best available sulphonamide, should be given at the first sign of capillary bronchitis with pyrexia or of otitis media. Large doses are necessary, for example 0.5 gramme (8 grains) four-hourly to an infant for three or four days, then 0.5 gramme six-hourly for four or five days. An oxygen tent is also of great value for a young child with pneumonia, and even in the uncomplicated disease is desirable for an infant under three months old. For convulsions, treatment by heat, lumbar puncture, and the oxygen tent is often effective, if not, an appropriate anaesthetic, for example a solution of 0.25 gramme (4 grains) pentothal sodium given intravenously in the jugular vein should be tried. If there is any evidence of active rickets, from 5 to 10 cubic centimetres of calcium gluconate, 10 per cent solution, should be injected intramuscularly, and ultra-violet light and vitamin D should be administered. Infectivity in whooping-cough has been shown by the cough plate method to be practically limited to four weeks. After this time children may be released from isolation even if they still occasionally whoop and vomit.

—II. STANLEY BANKS.

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YELLOW FEVER

See also B.E.M.P., Vol. XII, p. 660; and Cumulative Supplement, Key No. 1616.

Epidemiology and immunity

Immunity

Mouse-protection tests —E. C. Smith and J. W. Howie have performed the yellow fever mouse-protection test on 100 children under twelve years, from the Nigerian town which has the largest native population (389,907). Four mice were used for each test; if on the tenth day three were alive and well the reaction was considered to be positive. If two mice survived protection was accounted partial. Any other result was considered to be negative. Of the serums examined eleven gave full protection and nine gave partial protection. A better idea of the incidence of yellow fever among a native population is given by such a survey than by the number of recognized cases of the disease.

Virus and vectors

Inactivation of virus

Surface-active agents.—The use of living yellow fever virus for immunization has the drawback that the virus may become inactivated if exposed to heat, and virus inactivated by heat, by formaldehyde or by ultra-violet light fails to produce immunity unless given in enormous doses. G. M. Findlay has endeavoured to find a way out of the difficulty by using surface-active agents such as fatty acids and soaps to inactivate the virus. The material employed was mouse brain infected with the neurotropic strain of virus, and ground up in serum saline (1 in 10) to make a 20 per cent suspension; this was mixed with each of the substances to be tested in concentrations of 0.1, 0.2, 0.4, 1.0 and 2.0 per cent. The pH of the mixture was adjusted to from 7.0 to 7.2 with phosphate buffer and the whole was then incubated at 37° C. for two hours. Then 0.2 cubic centimetre of each mixture was injected intraperitoneally into

each of six mice which immediately beforehand had received an intracerebral injection of starch suspension. As controls, six mice were inoculated intraperitoneally with the suspension of infected mouse brain, and intracerebrally with starch suspension. The mice were kept under observation for three weeks and the dates of death of all that died were noted. An experiment was not recorded unless five of six control mice died of encephalitis within from five to ten days of inoculation. The results showed that many of the substances tested were capable of inactivating the yellow fever virus, although some did so only in concentrations which were also capable of causing toxic effects. The small number of compounds given below were found not only to inactivate the virus but also to allow it to retain some antigenic power: acetyl-salicylic, linoleic, linolenic, malic and mucic acids and 'tetralene'. A general law governing the phenomenon of inactivation could not be deduced from the chemical constitution of the substances tested.

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CUMULATIVE INDEX, 1939-44

A

Abdomen

acute

- diagnosis, (1944) 119
- differential diagnosis, malaria, (1940) 400
- pneumothorax therapy, during, (1940) 391
- rectus abdominis, spontaneous haemorrhage into, (1940) 413

periarthritis nodosa, (1940) 194

pain. *See* Abdominal pain

sensibility, (1940) 141

surgery,

anaesthesia in, (1944) 135

sympathetic nerves and, (1944) 85

wounds, (1943) 247

healing, (1940) 349

local anaesthetics in oil, effect of, (1940) 349

penetrating, (1940) 347

war, in, (1940) 11, (1944) 267

Abdominal

abscess from intestinal perforation, (1939) 181

aorta, embolism of, (1943) 125

diagnosis, (1939) 181

emergencies, in soldiers, (1943) 11

hyperaesthesia, cutaneous, in dyspeptics, (1941-1942) 215

pain,

acute abdominal emergencies, and, (1939) 181

diagnostic significance, (1940) 141

reno-urterial disease and reflex, (1944) 119

spinal appendicitis, (1941-2) 125

splanchnic anaesthesia, and, (1944) 85

pneumo-peritoneum, (1939) 181

sedimentation rate in diagnosis, (1939) 181

surgery, spinal anaesthesia in, (1940) 176

treatment, splanchnic anaesthesia, technique of, (1939) 181

voluntary muscular contraction, method for diminishing, (1939) 181

wounds, in war, (1940) 11

Abnormalities, congenital, surgical treatment, (1940) 14

Abortifacients, poisoning by quinine, (1940) 559

Abortion, (1939) 182

artificial, induction by male sex hormone, (1940) 142

cancer patients, abortifacient action of serum and urine from, (1940) 241

causes, vitamin C deficiency, (1940) 141

complications, *cf. welchii* and similar organisms, by, (1939) 182

diet in relation to, (1944) 22

dyscyesis, (1939) 158

habitual, (1941-2) 17

implantation of progesterone, (1941-2) 384

treatment of, (1939) 30

vitamin C therapy, (1940) 142

vitamin L in, (1940) 131, 142

incomplete, (1940) 141

conservative treatment of, (1941-2) 126

vaginal smear, diagnosis by, (1940) 141

induced,

male sex hormone, by, (1940) 142

tetanus following, (1941-2) 126

intentional and artificial, (1940) 142

medical grounds for, (1939) 182

natural, (1940) 141

artificial pyrexia, effect of, (1944) 120

causes, (1944) 120

prevention, (1940) 142

corpus luteum extracts, by, (1943) 333

spontaneous and induced, relative incidence of, (1941-2) 17

threatened,

aetiology and treatment, (1943) 15

implantation of progesterone, (1941-2) 384

subsequent fate of child, (1943) 16

vitamin E in, (1940) 130, 142; (1943) 16

Abortion—continued

threatened and habitual,

hormone therapy, (1944) 52

pregneninolone therapy, (1941-2) 126

treatment,

preventive, (1940) 142

vitamin C, (1940) 141

vitamin I, (1940) 142

unintentional and natural, (1940) 141

vitamin C in,

deficiency and, (1940) 141

therapy, (1940) 142

vitamin I in, (1940) 130, 142

Abortus fever

aetiology, (1940) 143

bacteriology, (1941-2) 126

laboratory infection in man, (1941-2) 126

milk, raw, as cause of, (1940) 143

morbid anatomy and sulphonamide treatment, (1939) 183

sulphonamides in, (1941-2) 126

treatment, sulphapyridine, (1940) 143

Abscess

breast, acute puerperal, (1944) 166

cerebellar, otogenic, (1943) 162

cerebral,

fungus infection and, (1941-2) 173

in relation to congenital heart disease, (1941-2) 174

otitis media complicated by, (1941-2) 217

pituitary tumour simulated by, (1944) 164

sella turcica region, in, (1944) 164

treatment, (1944) 164

epidural, of spine, (1941-2) 397

extradural, suppuration of middle ear complicated by, (1941-2) 216

lung, (1939) 410, (1940) 389

perinephric, (1943) 258

Acacia

nephrosis treated with, (1940) 422

nephrotic oedema treated with, (1941-2) 314

nephrotic syndrome treated with, (1943) 288

obstetric shock in, (1939) 395

Acalculia, (1943) 76

Acanthosis nigricans

associated with carcinoma, (1943) 103

distribution of lesions, (1943) 103

urticaria associated with, (1944) 120

Acapiin, splenomegaly after malaria treated with, (1940) 541

Acarnes, (1941-2) 390

Acarus scabiei, (1941-2) 391, (1943) 340 *See also* Scabies

Accessory sinuses of nose, (1939) 183

choanal congenital occlusion, (1939) 183

nasal sprays, (1939) 184

osteomas of maxillary sinus, (1939) 184

Accidents, alcoholism in relation to, (1939) 195

Acetanilide, poisoning, (1940) 554, (1941-2) 409

Acetarsol in dysentery amoebic, (1940) 136

Acetarsone, syphilis treated with, (1941-2) 404

Acetomenaphthone, (1943) 94

Acetyl- β -methylcholine

asthma treated with, (1941-2) 333

hypertension, in, (1940) 213

parasympathetic tropism of, (1941-2) 333

Acetyl- β -methylcholine bromide, megacolon treated with, (1940) 402, (1941-2) 303

Acetyl- β -methylcholine chloride, intravenous drip administration, (1941-2) 346

Acetylcholine

effect on heart, (1941-2) 333

labour, role in, (1940) 371

megacolon, as diagnostic test of utility of sympathectomy in, (1940) 402

nerve metabolism, relation to, (1939) 122, 164

vasospastic conditions of retinal arteries, in, (1939) 20

CUMULATIVE INDEX

- Acetylglarsenobenzene, syphilis treated with, (1941-2) 404
- Acetylsalicylic acid, stability of, (1940) 446
- Achalasia
cardia, of, (1944) 121
cardiac sphincter, of,
oesophageal ulcer and, (1940) 145
supervention of squamous-celled carcinoma, (1941-2) 128
treatment with nitrites, (1940) 146
cardiospasm and, (1940) 146
oesophageal, (1944) 121
treatment with nitrites, (1940) 146
pharyngo-oesophageal sphincter, of, (1941-2) 128 *See also* Plummer-Vinson syndrome
Plummer-Vinson syndrome, (1939) 185
Achar-Thiers syndrome, (1939) 192
- Achlorhydria
aetiology of, (1939) 185
leukaemia, in, (1939) 405
pernicious anaemia, and, (1940) 32, (1943) 47
- Acholuric jaundice *See also* Jaundice, acholuric
clinical picture, (1939) 206
splenectomy in, (1939) 207
steinal puncture in, (1939) 207, 248
- Achondroplasia
aetiology, (1940) 147
differential diagnosis, (1943) 104
material age, role of, (1940) 147
- Achrestic anaemia *See also* Anaemia, achrestic
splenectomy in, (1939) 204
- Achromia flava amyctica, (1939) 334
- Achropachyderma with pachyperostosis, (1943) 105
- Achylia gastrica, pernicious anaemia, and, (1943) 47
- Acidosis
blood in, (1941-2) 128
diabetic, treatment of, (1943) 187
rickets, late, relation to, (1944) 362
- Acne
blood-sugar in, (1940) 148
chlorinated naphthalene causing, (1944) 387
mental deficiency associated with, (1939) 431
treatment of, (1939) 185
cryotherapy, (1939) 185
testosterone propionate in, (1939) 186
tuberculin, (1939) 186
- Acne bacillus, culture of, (1943) 105
- Acne vulgaris
aetiology, (1940) 147
cryotherapy, (1941-2) 129
endocrine disorders, associated with, (1943) 104
iodine causing, (1940) 147
psychological reactions, (1941-2) 128
treatment,
calcium, (1940) 147, 148
insulin, (1940) 148
vitamin C, (1940) 147
vitamin D, (1940) 148
X-rays, (1944) 121
- Aconitine in rheumatism, (1939) 326
- Acoustic neurinoma, symptoms associated with, (1939) 96
- Acoustic neurofibroma, (1941-2) 174
- Acridiflavine
components, bacteriostatic values of, (1941-2) 330
infected wounds treated with hypertonic sodium sulphate and, (1941-2) 268
prevention of nasal sepsis and post-operative scarlet fever, in, (1941-2) 330
proflavine and, (1941-2) 330
- Acrocyanosis, cervico-thoracic sympathectomy for, (1941-2) 226
- Acrodermatitis chronica atrophans, carcinoma, in, (1943) 346
- Acrodynia, painless paronychia in, (1939) 441
- Acromegalism, (1943) 105
- Acromegaly
diabetes mellitus and, (1940) 148
differentiation from other changes of bone, (1943) 105
hyperparathyroidism secondary to, (1943) 105
pain in hands and feet, (1941-2) 129
pseudo-, (1943) 105
- Acromegaly—continued
treatment,
oestrogens, (1944) 122
- Acromion
apophysitis of, (1940) 296
bursitis, surgical treatment of, (1940) 300
- Acropachy, (1941-2) 274
- Acrosclerosis, Raynaud's phenomenon associated with, (1941-2) 374
- Actinomyces
bovis, (1940) 149
graminis, (1940) 149
moormani, (1940) 149
- Actinomycosis
abdominal, sulphonamide therapy, (1941-2) 129
bacteriology, (1940) 149
clinical picture, (1940) 149
ear, of, (1939) 323
Fallopian (uterine) tube, of, (1939) 339
generalized, (1940) 149
lacrimal concretions, (1940) 149
mycosis, (1940) 149
spinal, (1940) 149
treatment, (1940) 150
sulphanilamide, (1939) 186, (1940) 150
sulphonamides, (1941-2) 118, 129
surgical eradication, (1944) 112
thymol, (1939) 186
- Actinothrapy, (1940) 150, (1941-2) 129, (1943) 105
See also Ultra-violet irradiation
bactericidal power of, (1939) 187
- Adams-Stokes syndrome
electrocardiogram in, (1941-2) 246
heart block and, (1941-2) 246
- Addison's disease, (1939) 189, (1941-2) 131
adrenal cortical hormone in, (1939) 190
amyloid disease associated with, (1939) 189
cardiac failure after desoxycorticosterone, (1941-2) 132
clinical picture, (1940) 153, (1941-2) 131
course, (1940) 153
desoxycorticosterone in, (1939) 109, 166, (1940) 155
diabetes mellitus associated with, (1940) 153, (1943) 106
diagnosis, (1943) 106
value of potassium tolerance curve, (1941-2) 131
diet in (1939) 191
duration, (1940) 153
potassium in relation to, (1940) 154
progesterone, effect of, (1940) 155
sodium deficiency in, (1940) 113
treatment, (1939) 166, (1940) 153-5, (1944) 53
adrenal grafting, (1941-2) 132
cortical extract, (1940) 153-5
desoxycorticosterone acetate, (1940) 154; (1943) 107
sublingual administration of, (1941-2) 131
pellets, implantation of, (1941-2) 131
salt, (1940) 153
urinary excretion test in, (1943) 106
- Adenitis, inguinal, lymphopathia venereum causing, (1941-2) 300
- Adeno-acanthoma, uterus, of, (1940) 578
- Adenocarcinoma
appendix, of, (1944) 148
renal, complicating pregnancy, (1944) 278
thyroid gland, of, (1943) 224
vulva, of, (1943) 379
- Adenoids
operative technique, (1941-2) 130
radiographic diagnosis, (1940) 151
tonsils, enlarged, and, (1940) 553
X-ray therapy of, (1939) 187
- Adenoma
bronchial, (1941-2) 77, (1943) 60, 270, (1944) 67
chromophobe, of pituitary, (1940) 466
epididymis, of, (1943) 203
mammary, relation to gestation, (1939) 219
pancreas, of, (1939) 456, (1943) 245
pituitary, of, (1940) 466
sebaceous, (1943) 345
thyroid, of, (1939) 355

CUMULATIVE INDEX

Adenomyoma, of uterus, (1940) 288
 Adenopathy, giant follicular, and cutaneous lesions, (1943) 275
 Adie's syndrome, (1944) 149
 Adiponecrosis e frigore, (1941-2) 226
 Adiposity
 children, in, harmful effects of endocrine therapy, (1941-2) 130
 clinical picture, (1940) 152
 Dercum's disease, (1939) 188
 novocain infiltration, (1939) 188
 diet, (1939) 189
 dinitrophenol, cataract, relation to, (1939) 188
 genito-pituitary, (1939) 188, (1940) 152
 metabolism-stimulating hormone, (1939) 189
 treatment, benzedrine sulphate, (1940) 152, (1941-2) 130
 Adiposo-genital dystrophy, (1940) 152
 Adrenal
 cortex,
 Achar-Thiers syndrome, (1939) 192
 adrenalectomy, results of, (1939) 192
 adrenogenital syndrome, (1939) 191
 carbohydrate-regulating factor, (1943) 280
 carcinoma, primary, of, (1943) 107
 Cushing's syndrome, diagnosis from, (1939) 192
 deficiency, (1943) 280
 feminism in hyperfunction of, (1941-2) 133
 hyperfunction, (1939) 191, (1940) 155, (1941-2) 133, (1944) 122
 hyperplasia, (1940) 155, 156, (1941-2) 133
 neoplasm, and, (1943) 107
 hypertrichosis in female caused by, (1941-2) 243
 pseudo-hermaphroditism and, (1940) 155
 renal hypernephroma and virilism associated with, (1941-2) 133
 masculinization associated with adrenal cortical tumour of ovary, (1940) 156
 neoplasm, (1941-2) 133
 pseudo-sexual precocity, (1939) 192
 tumour of, radiographic diagnosis, (1940) 155
 cortical extract,
 Addison's disease, in, (1940) 153-5
 bromide eruptions treated with, (1941-2) 213
 confusional states, acute, in, (1940) 290
 crush injury treated with, (1943) 250
 hyperemesis gravidarum, in, (1940) 479
 osteitis deformans, in, (1940) 225
 pre-administration of, (1941-2) 387
 shock, in, (1940) 528
 due to burns, (1941-2) 181
 Adrenal deficiency, burns compared with, (1939) 268
 Adrenal glands, (1944) 53
 atrophy of, and spontaneous hypoglycaemia, (1941-2) 260
 carcinoma of mamma in relation to hormone of, (1939) 190
 potassium, in relation to, (1939) 190
 diabetes mellitus and hypertension treated by irradiation of, (1943) 152
 diseases, (1939) 189, (1940) 152-6, (1941-2) 131, (1943) 106, (1944) 122
 Addison's disease, (1939) 189
 grafting, in, (1941-2) 132
 hyperfunction, (1939) 191
 haemorrhage,
 acute bilateral, (1941-2) 132
 fatal, in pregnancy, (1941-2) 358
 meningococcal septicaemia associated with, (1941-2) 186
 hormones, (1944) 53
 hypoplasia and insufficiency, (1941-2) 131
 inclusion bodies in multiple carcinoma, (1944) 123
 melano-carcinoma, with widespread metastases, (1941-2) 133
 phaeochromocytoma, (1944) 123
 physiology, (1940) 152
 sympathetico-adrenal mechanism in migraine, (1943) 280
 tumours, (1941-2) 133; (1943) 107, 354; (1944) 123
 differential diagnosis, (1943) 108
 hypertension, paroxysmal, caused by, (1943) 150
 metastases simulating aneurysms, (1941-2) 133

Adrenal glands—*continued*
 tumours—*continued*
 neuroblastoma sympatheticum, (1943) 354
 radiographic diagnosis, (1940) 155
 Adrenal medulla
 anterior pituitary and, (1940) 152
 hyperfunction of, (1939) 193, (1943) 108, (1944) 123
 neuroblastoma, (1943) 108
 phaeochromocytoma, (1943) 107
 Adrenal secretions, role in shock, (1941-2) 386
 Adrenal virilism, (1943) 108
 Adrenalectomy
 effects in rats, (1941-2) 132
 results of, (1939) 192
 Adrenaline
 allergic conditions treated with, (1940) 164
 anaesthetics, local, effect on toxicity of, (1940) 176
 anti-convulsant effect, (1940) 446
 asthma, in, (1939) 200, 233
 continuous inhalation in, (1940) 203
 'slow', treated with, (1940) 204
 blood pressure changes due to, (1940) 447
 hay fever treated with, (1940) 161
 hypersensitivity, (1940) 448
 inversion of uterus treated with, (1940) 373
 leucocytosis, effect in producing, (1940) 447
 myasthenia gravis treated with, (1943) 285
 neurotic symptoms due to, (1940) 447
 pharmacology, (1939) 471
 procaine and, (1941-2) 112
 related compounds, (1940) 446
 suspension in oil, (1940) 161, 164
 tetany and, (1944) 316
 Adrenogenital syndrome, (1939) 191, (1944) 54
 Aerial contamination, (1944) 41
 Aerocele, cervical, (1941-2) 311
 Aero-otitis media, (1940) 49, (1941-2) 182
 Aerophagy, dyspepsia, in, (1944) 216
 Aerosols
 bactericidal agents, as, (1943) 53
 disinfection by, (1944) 41
 Age
 estimation from teeth and jaws, (1941-2) 303
 maternal, role in achondroplasia, (1940) 147
 old. See Old age
 peptic ulcer, relation to, (1941-2) 326
 Agglutination reactions
 glandular fever, in, (1940) 313, (1941-2) 235
 Rh factor, (1943) 148
 tularaemia, in, (1943) 369
 undulant fever, in, (1940) 573
 Agnosia, finger, (1943) 76
 Agranulocytosis
 aetiology, (1939) 193, (1940) 156, (1941-2) 134
 amidopyrine causing, (1939) 13, 193
 essential, (1939) 194
 gold therapy causing, (1940) 156
 pentnucleotide, treated with, (1939) 194
 sternal puncture in, (1939) 248
 sulphapyridine causing, (1940) 156, (1941-2) 134, 343
 sulphathiazole causing, (1941-2) 134
 sulphonamides causing, (1939) 32, 177, 193, (1943) 109
 treatment, (1939) 193
 Anthum, case in Great Britain, (1943) 109
 Air
 disinfection by aerosols and gaseous chemicals, (1944) 41
 dust-borne organisms in, (1941-2) 185
 embolism. See Embolism, air
 hospitals, irradiation of, in, (1941-2) 130
 pathogenic organisms in, (1944) 41
 radiant disinfection of, (1943) 105
 sterilization of, (1944) 63
 ultra-violet irradiation of, (1940) 150, (1944) 42
 warm moist, in treatment of burns, (1940) 237
 Air-borne and direct infection, (1943) 52, 54
 Air-borne infection, diphtheria, (1941-2) 209
 Airplane flights, whooping-cough treated by, (1944) 408
 noise, hearing, effect on, (1940) 206
 Air-raids
 casualties, (1940) 9
 blast injuries of lungs, (1941-2) 297

CUMULATIVE INDEX

Air-raids—continued

Casualties—continued

- blood transfusion for, (1943) 158
- crush injuries, (1941-2) 269
- psychiatric, (1941-2) 363
- surgery of, (1941-2) 265
- X-ray examination, (1941-2) 371
- effects on civilians, (1941-2) 363, (1944) 341
- mental reactions to, (1943) 314
- period of intensive, (1944) 5
- precautions, (1944) 8
 - gas attack, (1944) 8
 - homeless, care of, (1944) 8
 - shelters, (1944) 8
- shock, (1943) 314
- Air-sickness, (1941-2) 36
- Air Training Corps, mass radiography in, (1943) 319
- Air transport, evacuation of wounded by, (1943) 8
- Albright's syndrome, (1944) 162
- Albucid, (1939) 171, (1940) 133, (1943) 99
 - burns treated with, (1941-2) 182
 - chemistry and pharmacology of, (1939) 170
 - gonorrhoea treated with, (1939) 357 (1940) 319, (1941-2) 237
- soluble, (1943) 99
- Albumin
 - fractions, (1940) 121
 - serum, in, (1940) 121
- Albuminuria
 - aetiology, (1939) 194
 - diphtheria, in, significance of, (1939) 312
 - orthostatic, (1943) 110
 - pregnancy, in, (1940) 17
 - recruits, in, (1943) 110
 - scabies examined for, (1939) 194
- Alcohol
 - antiseptic properties of, (1939) 384
 - cirrhosis of liver and coproporphyrinuria, (1944) 245
 - denatured, hypoglycaemia due to, (1943) 110
 - excretion in urine, (1941-2) 134
 - injection,
 - aural vertigo treated with, (1943) 376
 - migrainous neuralgia, in, (1941-2) 307
 - thrombo-angitis obliterans, in, (1939) 225
 - lavage, acute peritonitis treated with, (1941-2) 330
 - methyl alcohol poisoning, (1943) 110
 - subarachnoid injections of, for pain in cancer, (1941-2) 185
 - toxic effects of, (1940) 157, (1941-2) 134, (1943) 110, (1944) 123
- Alcoholic
 - beri-beri and vitamin B deficiency, (1941-2) 135
 - delirium, acute, (1943) 110
 - encephalopathy, nicotinic acid in treatment, (1943) 64
 - gastritis, (1943) 46
 - oesophagitis, (1941-2) 134
 - psychoses, (1940) 497; (1941-2) 369
- Alcoholism, (1939) 194, (1941-2) 134, (1943) 110, (1944) 123
 - accidents, relation to, (1939) 195
 - amaurosis, alcoholic, (1939) 195
 - cerebrospinal fluid pressure in, (1941-2) 188
 - coramine in treatment, (1939) 195
 - delirium tremens, treatment of, (1939) 195
 - fatadic shock therapy, (1943) 111
 - gastritis caused by, (1941-2) 135
 - hepatic cirrhosis caused by, (1939) 196
 - hepatitis, chronic, as cause of, (1939) 409
 - hepatosis, pre-cirrhotic, (1941-2) 135
 - kidneys, effect on, (1939) 196
 - Korsakow's syndrome, (1939) 196
 - psychological effects, (1940) 157
 - sclerosis corticalis laminaris alcoholica, (1939) 196
 - tolerance tests, (1939) 194
 - treatment, (1939) 197
 - conditioned reflex, establishment of, (1940) 158
 - glucose and insulin, (1940) 157
 - nicotinic acid, (1940) 157
 - vitamin B, in cardiac complications, (1939) 197
 - vitamin B₁, (1940) 157
 - war-time, in, (1940) 280
- Wernicke's disease (encephalitis haemorrhagica superior), (1939) 196

Alcoholism, acute, (1940) 157 *See also* Delirium tremens

- child, in, (1940) 158
- effect on vision, (1941-2) 134
- estimation of alcohol in urine, (1941-2) 134
- hypoglycaemia as sequel, (1944) 123
- treatment, (1944) 124
- Alcoholism, chronic, (1939) 196
 - beri-beri and vitamin B deficiency, (1941-2) 135
 - cerebral changes, (1941-2) 134
 - diagnosis, in surgical patients, (1940) 158
 - oesophagitis in, (1941-2) 134
 - pellagra and, (1941-2) 324
 - surgical patients, in, (1940) 158
 - treatment, (1944) 123
 - general management, (1944) 123
 - psychotherapy, (1944) 123
- Alexia, (1943) 76
- Alimentary diseases, (1941-2) 3
- Alimentary tract
 - diseases, (1939) 43, (1940) 25, (1941-2) 24
 - abuse of purgatives—a clinical entity, (1939) 50
 - advances in, (1944) 30
 - anorexia nervosa, (1939) 45
 - biliary drainage in diagnosis of gall-bladder disorders, (1939) 48
 - gastric and duodenal ulcers, treatment of, (1939) 46
 - gastrosocopy, (1939) 47
 - haematemesis, treatment of, (1939) 47
 - oesophagus, simple ulcer of, (1939) 43
 - regional ileitis (1939) 49
 - upper dysphagia with anaemia (Paterson's syndrome), (1939) 43
 - infection in lymphopathia venereum, (1941-2) 300
 - surgical disease of, (1940) 12
 - X-ray examination, (1944) 356
- Alkaline diet and sodium bicarbonate in urticaria, (1939) 201
- Alkaline powder excessive use of, in gastric ulcer, (1941-2) 135
- Alkalis
 - aluminium hydroxide and magnesium trisilicate as (1939) 167
 - excessive administration of, (1939) 167
 - peptic ulcer treated with, (1940) 439
 - renal calculi following use of, (1940) 366, 442
 - use in induction of labour, (1941-2) 279
- Alkaloids
 - poisoning, (1940) 556
 - toxicology (1941-2) 409
- Alkalosis, (1940) 159
 - alkaline treatment causing, (1941-2) 135
 - biochemical test for, (1939) 198
 - cerebrospinal fluid in, (1940) 159
 - clinical picture, (1940) 159
 - diabetes complicated by, (1939) 309
 - morbid anatomy, (1940) 159
 - renal changes (1940) 159
- Alkaptonuria, (1939) 267, (1943) 111
- hyperuricaemia associated with, (1944) 124
- Alkaptonuric ochronosis, (1943) 111
- Allergens
 - bacterial, sensitization to, in dermatitis herpetiformis, (1941-2) 204
 - gastro-intestinal allergy, in, (1940) 163
 - house dust, in, (1944) 125
- Allergy
 - dermatitis, protamine zinc insulin causing, (1943) 187
 - diseases, (1944) 126 *See also* Allergy
 - eczema,
 - cataract and, (1941-2) 137
 - infants, of, (1941-2) 137
 - reactions, blood donors, in, (1943) 30
 - rheumatism, (1943) 112
- Allergy, (1939) 198, (1941-2) 135, (1943) 111, (1944) 125
 - aetiology, (1940) 159
 - biochemistry, and, (1939) 198
 - pathogenesis, and, (1943) 112
 - pathology, and, (1941-2) 136
 - allergens in house dust, (1944) 125
 - anaphylaxis, (1939) 198
 - atelectasis in children, role in, (1940) 388

CUMULATIVE INDEX

Allergy—continued

- bee stings, (1940) 160
 - blood histamine variations, (1943) 112
 - bronchiectasis, relation to, (1939) 265
 - butyn, (1939) 199
 - catarrhal jaundice, relation to, (1939) 389
 - cold, (1940) 163
 - colitis, ulcerative, and, (1943) 176, (1944) 183
 - dermatitis, (1940) 163
 - herpetiformis possibly due to, (1939) 300
 - diagnosis, (1941-2) 136, (1944) 125
 - disseminated sclerosis and, (1940) 277
 - eczema of infants, (1939) 198
 - erythema nodosum, suggested cause of, (1939) 336
 - extracts, dried, in naturalization tests, (1944) 125
 - food, (1941-2) 138
 - fungus infections causing, (1941-2) 137
 - gastro-intestinal, (1940) 163
 - milk as cause of, (1941-2) 138
 - genito-urinary manifestations, (1940) 164
 - histaminase skin tests, (1941-2) 136
 - histamine, role of, (1941-2) 136
 - hyperplastic disease of respiratory tract, relation to, (1940) 160
 - insulin, (1940) 160
 - karaya (Indian) gum, (1940) 160
 - manchineel poisoning, (1939) 199
 - menthol in, (1939) 199
 - milk as cause of, (1941-2) 138
 - mosquito bites, (1940) 160
 - naturalization tests, use of dried extracts, (1944) 125
 - plasma potassium in, (1940) 113
 - respiratory tract, hyperplastic disease of, (1940) 160
 - skin, of, (1941-2) 137, (1943) 112
 - fungus disease causing, (1941-2) 137
 - histaminase in treatment, (1941-2) 137
 - skin manifestations, treatment, (1940) 163
 - treatment, (1944) 125
 - adrenaline in oil, (1940) 161, 164
 - histaminase, (1940) 161 4, (1941-2) 137
 - histamine azo-protein, (1943) 112
 - hormones, (1944) 125
 - pollen desensitization, (1943) 112
 - potassium chloride, (1941-2) 136
 - potassium salts, (1940) 161, 164
 - propadine hydrochloride, (1940) 164
 - water balance, role of, (1940) 159
- Aloes ointment, burns treated with, (1940) 237
- ## Alopecia
- actiology, (1940) 165
 - endocrine factor, (1944) 128
 - peroneal region, of, (1940) 165
 - totalis,
 - ocular changes, with, (1944) 128
 - pituitary dysfunction in relation to, (1940) 165
 - pregnancy, during, (1940) 165
 - treatment, endocrine therapy, (1940) 165
- ## Alopecia areata
- neurotrophic origin, (1943) 113
 - treatment, endocrine therapy, (1940) 165
- ## Altitude
- effect on intraocular volume, (1941-2) 160
 - high,
 - erythraemia as caused by, (1939) 336
 - intra-ocular pressure at, (1941-2) 160
 - whooping-cough treated by, (1944) 408
 - sickness, (1941-2) 32
- ## Alum-precipitated insulin, (1940) 266
- ## Alum-precipitated toxoid, diphtheria immunization, in, (1943) 191
- ## Aluminium fluoride, toxic effects of, (1940) 560
- ## Aluminium hydroxide
- antacid, as, (1939) 167
 - colloidal, peptic ulcer, in, (1939) 468, (1940) 439, (1941-2) 327
 - intra-gastric drip method, (1940) 440
 - colloidal kaolin, and, as vaginal cleanser, (1940) 593
 - peptic ulcer treated with, (1941-2) 327, (1944) 32
- ## Aluminium phosphate gel, peptic ulcer treated with, (1941-2) 327
- ## Aluminium silicate (kaolin), peptic ulcer treated with, (1939) 22

- Alzheimer's disease, (1943) 113
 - actiology and pathology, (1939) 202
 - clinical picture, (1940) 166, (1944) 129
 - morbid anatomy, (1940) 166, (1944) 129
- ## Alzheimer's tangles, (1943) 113
- ## Amaurosis
- alcoholic, (1939) 195
 - fugax, (1940) 206
- ## Amaurotic family idiocy, congenital, (1943) 172
- ## Amblyomma hebraeum, vector of tick-bite fever (1940) 81
- ## Amblyopia, toxic, vitamin B in treatment of, (1939) 244
- ## Ambulance services, (1944) 5
- ## Amenorrhoea
- actiology, (1940) 166
 - hormone therapy, (1944) 51
 - secondary, (1940) 166
 - treatment of, (1939) 202
 - progesterone, (1943) 114, 334
 - prostigmin, (1940) 166
 - stilboestrol, (1940) 522
 - tuberculosis, association with, (1940) 166
- ## Amethocaine hydrochloride, (1941-2) 113, (1944) 110
- ## Amidopyrine (pyramidon), agranulocytosis caused by, (1939) 13, 193
- dermatitis caused by, (1940) 257
 - nephritis, in treatment of, (1939) 444
- ## Amines, toxic, and hepatic disorders, (1940) 54
- ## Amino-acetic acid, effect on muscular fatigue, (1941-2) 331
- ## Amino-acids
- food, in, (1941-2) 232
 - nephrotic crisis, deficiency in blood, (1940) 421
- ## Amino-derivatives, poisoning by, (1940) 562
- ## Aminophyllin
- anaemia treated with, (1940) 448
 - asthma treated with, (1940) 203
 - peripheral blood flow, effect on, (1941-2) 331
 - treatment, in,
 - angina pectoris, of, (1941-2) 144
 - asthma, of, (1939) 233
 - bronchial spasm, of, (1941-2) 158
- ## Ammonia, poisoning by, (1943) 363
- ## Ammoniated mercury ointment, generalized exfoliative dermatitis caused by, (1943) 364
- ## Idiosyncrasy in children, (1941-2) 332
- ## Ammonium chloride,
- control of bismuth therapy by, (1941-2) 404
 - convulsion therapy, in, (1940) 59, (1944) 349
 - convulsion therapy in mental disorders, in, (1941-2) 368
 - lime burns of conjunctiva, in, (1939) 289
 - Meniere's syndrome treated with potassium nitrate and, (1940) 584
- ## citrate, trichuriasis, treated with iron and, (1940) 420
- mandelate, (1941-2) 112
 - salts as expectorants, (1941-2) 178
 - tartrate, lime burns of eye treated with, (1942) 147
- ## Amnioplastin, use in surgery, (1941-2) 264
- ## Amniotic fluid, pulmonary embolism caused by particles from, (1943) 261
- ## Amniotic membrane, head injuries, use in, (1940) 348
- ## Amoebiasis, (1940) 167
- Balantidium coli* infection and, (1940) 167
 - clinical picture, (1940) 167
 - cutis, (1941-2) 138
 - diagnosis, (1940) 167
 - pathology, (1940) 167
 - protozoology, (1940) 167
- ## Amoebic
- abscess. *See* Liver, amoebic abscess
 - dysentery. *See also* Dysentery, amoebic treatment, (1943) 114
- ## Amphetamine, (1943) 93 *See also* Benzedrine
- ## Amphetamine sulphas, (1943) 93
- ## Amputation
- anaesthesia, choice of, (1943) 114
 - complications, (1940) 168
 - crush injuries, in, (1943) 249
 - general principles, (1943) 115

CUMULATIVE INDEX

Amputation—*continued*

- guillotine method, controversy about, (1940) 11
- ligature of femoral vein in, (1940) 395
- pain after, vitamin B₁₂ in treatment, (1940) 168
- procaine hydrochloride in phantom-limb pain, (1939) 202
- refrigeration and tourniquets, (1943) 114
- spontaneous, of tongue, (1940) 411
- Amylase
 - activity of duodenal contents in infants, (1944) 263
 - test, pancreatic disease, in (1944) 20
 - urinary, estimation of, (1940) 575
- Amyl nitrite
 - bronchial tree, effect on, (1940) 448
 - cardiospasm, treated with, (1940) 146
 - spasm and colic, in, (1939) 165
- Amyloid disease, (1941–2) 138
 - localized, of skin, (1943) 115
 - nervous system, of, (1943) 116
 - primary systemic, (1943) 115
- Amyloid tumour, larynx, of, (1943) 41, 262
- Amylotrophic lateral sclerosis, vitamin B₆ therapy, (1941–2) 428
- Amyotonia congenita, vitamin E in, (1940) 131
- Amyotrophic lateral sclerosis, (1943) 281, (1944) 304
- vitamin E therapy, in, (1940) 70, 131, 409, (1941–1942) 307, 428, (1944) 89
- Amytal, (1939) 163
 - as prognostic test in shock therapy, (1944) 74
- Anabolin, hypertension treated with, (1943) 152
- Anacardone, (1939) 164
 - nikethamide, official name for, (1940) 127
- Anaemia, (1939) 203, (1941–2) 139, (1943) 116
 - acholuric jaundice, in, (1939) 206
 - sternal puncture in, (1939) 207, 248
 - achrestic, (1939) 204, (1940) 33, 170, (1943) 23
 - restricted use of name, (1943) 116
 - splenectomy in, (1939) 204
 - ankylostomiasis, in, (1940) 187
 - aplastic, (1939) 206, (1943) 117
 - aetiology and treatment, (1943) 117
 - idiopathic, treatment by intrasternal introduction of bone marrow, (1941–2) 141
 - pathology, (1943) 118
 - sternal puncture in, (1939) 248
- Baghdad spring, (1941–2) 140
- blood loss causing, (1941–2) 139, (1943) 118
- causes and treatment, (1943) 23
- classification of, (1940) 4, 6
- coeliac disease, in, (1939) 282
- Cooley's erythroblastic, (1940) 172, (1941–2) 140
- deficiency, in women and infants, (1944) 22
- dysphagia associated with (Paterson's syndrome), (1939) 43
- erythroblastic, (1941–2) 140
- erythrophagocytic, (1941–2) 140
- haemolytic, (1941–2) 139, (1943) 26, 118, (1944) 132
 - acute or subacute, (1941–2) 140
 - atypical, (1940) 171
 - bones in, (1940) 171
 - chronic, with haemoglobinuria, (1941–2) 140
 - familial haemolytic, (1941–2) 139, (1944) 133
 - Lederer's, (1941–2) 140
 - differential diagnosis in pregnancy, (1944) 132
 - sulphonamide therapy causing, (1943) 118
 - terminating carcinoma of stomach, (1941–2) 401
 - new-born, of, (1943) 24, 119
 - erythrophagocytosis in, (1939) 206
 - refractory, (1944) 133
 - sulphonamides causing, (1939) 177, (1940) 120
 - haemolytic neonatorum, (1941–2) 140
 - haemorrhage causing, (1943) 118
 - Hodgkin's disease, in, (1940) 343
 - hyperchromic macrocytic, Hodgkin's disease, in, (1940) 343
- hypochromic
 - deficiency, (1941–2) 139, (1944) 131
 - chlorosis, (1943) 117
 - of infancy, incidence, aetiology and treatment, (1939) 205
 - idiopathic, (1943) 117
 - infancy, of, (1943) 116

Anaemia—*continued*

- hypochromic—*continued*
 - microcytic, (1943) 117
 - pregnancy, of, (1939) 205; (1940) 171
- idiopathic aplastic, treatment of, (1941–2) 141
- hypochromic, (1940) 6; (1944) 131
- infantile blood transfusion in, (1939) 250
- iron in treatment of, (1940) 6
- macrocytic, sternal puncture in, (1939) 247
- hyperchromic, of pregnancy, clinical picture, (1944) 131
- megalocytic, (1939) 204
 - after gastro-enterostomy, (1943) 116
 - pregnancy, of,
 - aetiology, (1940) 171
 - incidence, (1944) 130
 - symptoms, (1944) 130
 - treatment, (1944) 130
 - tropical, (1939) 204
- myxoedema, associated with, (1939) 53
- nutritional, (1944) 131
 - children, in, (1943) 215
- obscure types, (1943) 23
- pernicious, (1939) 203 *See also* Pernicious anaemia
 - leukaemia associated with, (1939) 405
- porphyrin excretion in, (1943) 25
- post-haemorrhagic, (1941–2) 139
- pregnancy, in, (1940) 187, (1944) 22
- recent work on, (1944) 129–34
- refractory, (1943) 23, 117
 - secondary, caused by sulphanilamide, (1941–2) 344
- sickle-cell, (1943) 118, (1944) 132
- survey of, (1939) 53
- treatment, (1944) 133
 - blood transfusion, (1940) 222
 - concentrated suspension of red cells, (1941–2) 168
 - war-time, in, (1944) 133
- Anaerobic infection, knowledge of, gained in war, (1940) 3
- Anaesthesia, (1939) 207, (1941–2) 142; (1943) 120, (1944) 135
 - abdominal surgery, in, (1944) 135
 - anaesthetics, relative safety of, (1940) 109
 - anoxia during, (1940) 173
 - apparatus, (1944) 137
 - avertin, (1941–2) 142
 - basal narcosis, (1939) 210, (1940) 177, (1941–2) 142, (1944) 136
 - contra-indications and uses, (1944) 136
 - hexobarbitone soluble (evipan sodium) (1941–1942) 142
 - narcotics, (1939) 210
 - pentothal sodium, (1944) 137
 - premedication, (1939) 210
 - caudal, in labour, (1943) 18, (1944) 281
 - children, in, (1940) 111
 - pre-anaesthetic sedatives for, (1941–2) 143
 - chloroform, (1940) 109
 - choice of anaesthetic, (1939) 207
 - amputation, for, (1943) 114
 - shock, in, (1941–2) 388
 - combined methods, (1939) 212
 - convulsions, in, (1940) 174
 - coramine as antidote for inhalation anaesthetics, (1939) 212
 - cyclopropane, (1939) 208, (1940) 109; (1944) 137
 - dental surgery, in, (1939) 207
 - diet, pre-anaesthetic, (1940) 110
 - diethyl ether, (1940) 109
 - diothane hydrochloride for urethral anaesthesia, (1939) 209
 - divinyl ether, (1940) 109
 - dosage, (1944) 138
 - electrical, (1940) 110
 - endotracheal, (1940) 173
 - children, in, (1940) 111
 - dental surgery, in, (1939) 207
 - ether, (1939) 207 *See also* Ether anaesthesia
 - convulsions during, (1943) 120
 - ethyl *n*-propyl ether, (1940) 175
 - fatalities, (1944) 138
 - general practitioner and, (1944) 135

CUMULATIVE INDEX

Anaesthesia—continued

- infants, in, (1940) 111
 - inhalation, (1940) 172
 - intravenous, (1941-2) 143
 - labour, in, (1941-2) 280
 - caudal anaesthesia, continuous, (1944) 281
 - local,
 - adrenaline, and toxicity of, (1940) 176
 - fibrositis treated with, (1943) 208-10
 - herpes zoster treated with, (1941-2) 256
 - minor fractures treated with, (1940) 276
 - muscular rheumatism treated by injection of, (1941-2) 229
 - novocain, fibrositis treated by, (1940) 7
 - pantocaine in, (1939) 210
 - procaine, ocular sensitivity to, (1941-2) 338
 - procaine hydrochloride, (1941-2) 142
 - medico-legal aspects, (1939) 212
 - mortality, (1944) 138
 - nitrogen monoxide and oxygen, (1941-2) 282
 - nitrous oxide, (1940) 111, (1943) 120 *See also* Nitrous oxide anaesthesia
 - opium as pre-anaesthetic sedative, (1941-2) 143
 - Oxford vaporizers, (1944) 137
 - oxygen supply during and after, (1940) 110
 - pentothal sodium,
 - intermittent administration, (1944) 137
 - uses and dangers, (1944) 137
 - perineal, in labour, (1941-2) 280
 - post-operative chest complications, (1940) 108
 - pre-anaesthetic sedatives, (1941-2) 143
 - pulmonary complications, (1940) 108
 - recent work on, (1940) 108
 - rectal, (1941-2) 142, (1944) 136
 - basal narcosis, and, (1943) 121
 - respiration, and, (1940) 172
 - safety, in, (1944) 138
 - spinal, (1939) 209
 - abdominal surgery, in, (1940) 176
 - blood pressure, in, (1940) 176
 - cardiospasm treated by, (1940) 146
 - congenital megacolon treated by, (1940) 146
 - convulsion therapy, in, (1944) 349
 - headache following, (1940) 110
 - maintenance of blood pressure during, (1941-2) 142
 - neossynephrin for maintaining blood pressure, (1941-2) 142
 - neossynephrin premedication, (1939) 209
 - nupercaine, (1944) 136
 - parendrine, use of, (1940) 176
 - procaine technique, (1939) 209
 - pulmonary tuberculosis, in, (1944) 136
 - urinary retention after, (1941-2) 162
 - spinal, (1944) 84
 - abdominal pain and, (1944) 85
 - technique and conditions treated by, (1939) 181
 - surgery, in, (1939) 25
 - vaporizers, Oxford, (1944) 137
 - vertebral column, procedures around, (1944) 85
 - vinyl ether, (1939) 208
 - convulsions during, (1940) 175
 - war surgery, in, (1943) 8
- Anaesthetics, local, in oil, use in abdominal wounds, (1940) 349
- Anaesthetists, training of, (1944) 135
- Anahaemin, in tropical megalocytic anaemia, (1939) 204
- Anal canal, carcinoma, squamous-celled, (1941-2) 147
- Analgesia, in labour, (1941-2) 280
- Anaphylactic purpura, regional ileitis, acute, simulated by, (1943) 180
- Anaphylaxis
 - cause of, (1939) 198
 - periarteritis nodosa and, (1944) 151
- Anastomosis, soluble rod method of vascular, (1941-2) 264
- Androgens, (1944) 47
 - alopecia and, (1944) 129
 - calvities and, (1944) 129
 - cancer tissue, effects on, (1941-2) 183
 - dysmenorrhoea, relation to, (1944) 211
 - excretion, rate of, (1941-2) 384
 - gynaecology, in, (1944) 27

Androgens—continued

- involuntarily psychoses treated with, (1944) 347
 - 17-ketosteroid assay, (1944) 48
 - testicular, role in carcinoma of prostate, (1944) 336
 - urinary, (1944) 47
- Androsterone, desoxycorticosterone, androgenic effect of, (1940) 525
- Aneurin, administration in diabetes mellitus, (1941-2) 206
- conditions cured by, (1939) 18
- Aneurin hydrochloride, (1940) 128 *See* Vitamin B₁
- Aneurysm, (1939) 213, (1940) 179-81, (1943) 121, (1944) 139
 - aortic, (1939) 213, (1940) 179, (1941-2) 143
 - abdominal, (1941-2) 143
 - diagnosis, (1941-2) 143
 - syphilis causing, (1941-2) 143
 - dissecting, (1943) 122
 - pulmonary stenosis and, (1941-2) 143
 - rupture into pulmonary artery, (1943) 122
 - rupture of thoracic aorta, (1943) 122
- arteriovenous, clinical types and treatment, (1944) 139
- cardiac, (1939) 214
- carotid, (1940) 180
 - internal, causing aural haemorrhage, (1941-2) 144
- cerebral,
 - congenital, (1940) 181
 - rupture with ipsilateral signs, (1943) 123
- cirsoid, (1943) 123
- coeliac artery, with symptoms of acute cholecystitis, (1941-2) 143
- common carotid, (1940) 180
- congenital intracerebral, (1940) 181
- dissecting, (1940) 179
 - adolescent, in, (1940) 180
 - post-mortem evidences, (1944) 139
 - secondary to renal calcification, (1941-2) 144
- spinal cord ischaemia in, (1943) 123
- innominate artery, (1940) 180
- internal carotid, (1941-2) 144
- intracerebral, congenital, (1940) 181
- intracranial, surgical treatment, (1943) 123
- metastases from hyaline nephroma simulating, (1941-2) 133
- peripheral, (1939) 214, (1941-2) 144, (1943) 123
 - clinical types and treatment, (1944) 139
- pulmonary
 - artery, (1939) 214, (1941-2) 144
 - syphilis causing, (1944) 139
- renal, rupture during pregnancy, (1944) 25
- splenic, rupture during pregnancy, (1944) 25
- splenic artery, of, (1941-2) 398
- Angina
 - throat, associated with mononucleosis, (1941-2) 235
- Vincent's, (1943) 2 *See also* Vincent's angina
- Angina pectoris, (1939) 215, (1941-2) 144
- acute ischaemia of myocardium as cause of, (1939) 215
- aetiology, (1940) 181
- anaemia, pernicious, complicating, (1940) 169
- angina of effort, electrocardiographic changes in, (1939) 215
- clinical picture, (1940) 182
- coronary thrombosis, and, (1939) 215
- cull test, (1939) 216
- effort, of, hypothyroidism as cause of, (1944) 46
- electrocardiography in coronary diseases, (1939) 215
- myxoedema associated with, (1940) 181
- myxoedema, in, (1944) 307
- myxoedematous hypothyroidism, (1939) 215
- nicotine poisoning resembling, (1939) 215
- pain, (1941-2) 144
 - pathology and pathogenesis, (1940) 182
 - treatment with drugs, (1940) 182
- thyroid dysfunction in, (1940) 181
- thyroidectomy in treatment, (1939) 216
- treatment, (1940) 182-4
 - aminophylline, (1941-2) 144
 - cardio-omentopexy, (1940) 183
 - drugs, (1940) 182
 - elastic supporting belt in obesity, (1940) 184

CUMULATIVE INDEX

- Angina pectoris**—*continued*
treatment continued
 ligation of vena coudis magna, (1943) 124
 surgical, (1940) 183
 sympathectomy, (1940) 184
 testosterone propionate, (1943) 124, (1944) 140
 thyroidectomy, (1940) 183, 338
- Angiography, cerebral**, (1940) 103
- Angioma**, (1939) 218
 familial cerebellar, (1943) 127
 hepatic disease, associated with, (1939) 218
 larynx, of, (1943) 40
 mesodermal, of eye, (1943) 205
 port wine birth-marks, Grenz-ray therapy, (1940) 187
 radium therapy, (1939) 218
 renal papilla, in, (1943) 229
 treatment, radium, (1940) 186
- Angiomatosis retinae**
 treated by catholysis and surface diathermy, (1941-2) 377
 X-ray therapy, (1940) 385
- Angioneurotic oedema**, histaminase, treatment with, (1940) 163
- Angioreticuloendothelioma**, (1943) 235
- Angiotonin**
 effects of, (1943) 150
 role in hypertension, (1941-2) 165
- Angular depth perception apparatus**, (1941-2) 31
- Anhydro-hydroxy-piogestione**, (1943) 95
- Androsis**, (1941-2) 147
- Anilism**, (1943) 6
- Aniseikonia**, (1939) 337
- Ankle**
 coxoidial arthritis of, (1943) 146
 fracture, osteoarthritis as complication of, (1941-1942) 211
 tuberculous, treatment of, (1941-2) 274
- Ankylosing spondylitis**, (1941-2) 155
- Ankylostomiasis**, (1939) 218
 anaemia in, (1940) 187
 iron and blood transfusion in, (1940) 187
 nervous complications, (1940) 187
 pancreatic necrosis caused by, (1939) 455
 peripheral polyneuritis associated with, (1939) 218
 tetraachlorethylene in treatment of, (1939) 219
 vitamin B₁ deficiency in, (1939) 218
- Anonychia**, partial, with bony changes, (1941-2) 230
- Anopheles gambiae**, carrier of malaria, (1940) 76
- Anopheles maculipennis-atroparvus**, carrier of malaria, (1940) 75
- Anorchidism**, (1941-2) 231
- Anorexia nervosa**, (1939) 219
 aetiology and treatment, (1939) 45
 clinical picture, (1944) 141
 obesity, pathological, as sequel, (1944) 141
 Simmonds's syndrome, differential diagnosis from, (1939) 219, (1943) 340
 vitamin K deficiency in, (1944) 404
- Anosognosia**, (1943) 75
- hemiplegia**, in, (1943) 241
- Apnoxaemia**
 aminophylline in, (1940) 448
 aviators, in, (1943) 140
 nitrous oxide anaesthesia causing, (1943) 120, (1944) 136
- Anoxia**
 adrenal cortex, role of, (1943) 280
 anaesthesia causing, (1943) 120
 anaesthesia, during, (1940) 173
 aviators, in, (1941-2) 32, (1943) 139
 cerebral, (1944) 159
 convulsion therapy, in, (1940) 58
 lung tumours, primary, and, (1940) 240
 mental disease, in, (1940) 54
 schizophrenia, in, (1943) 64
- Antacids**, (1939) 167 *See also* Alkalis
 gastric acidity, effects on, (1940) 439
- Antenatal care**, (1939) 37, 219, (1940) 187, (1944) 142
 diet, (1939) 220, (1944) 22, 142-5
 hypovitaminosis B₁ and E, (1944) 142
 mammary gland, pathology of, (1939) 219
- Anthelmintic**, phenothiazine as, (1941-2) 122
- Anthracene**, carcinogenetic effects of, (1943) 171
- Anthracite dust**, effect on tubercle bacilli, (1941-2) 415
- Anthracosis**, cardiovascular system in, (1940) 188
- Anthrax**, (1943) 94
 serum, (1943) 94
 meninges, (1940) 188
 sulphonamide compounds in, (1940) 188
 treatment,
 arsenic with sulphapyridine, (1943) 128
 serum and neokhaisgan, (1941-2) 147
- Antibodies**, in poliomyelitis, (1941-2) 356
- Anticoagulant**, cysteine hydrochloride, (1940) 451
- Anticonvulsant**
 adrenaline as, (1940) 446
 sodium-diphenylhydantoinate, (1940) 454
- Antigen**
 detoxified, in whooping-cough, (1940) 595
 trichiniasis, in diagnosis of, (1944) 390
 whooping-cough treated with, (1941-2) 431
- Antihormones**, (1944) 44
- Antimony**
 kala-azar, in, (1943) 256
 oriental sore treated with, (1944) 284
- Anti-pressor substance**, hypertension, in, (1943) 149
- Anti-prothrombin**, thrombosis, in, (1943) 375
- Antipyretic drugs**, cancer treated by, (1941-2) 339
- Antipyrates**, porphyrin excretion and, (1940) 324
- Antipyrin** in labour, (1939) 397
- Antiseptic emulsions**, wounds treated by, (1943) 248
- Antiseptic snuff**, (1941-2) 331, (1943) 305
- Antiseptics**, (1941-2) 10
 barberry root, (1941-2) 332
 boric acid, (1944) 13
 chlorophyll, (1941-2) 333
 flavines, (1944) 13
 historical survey, (1944) 320
 penicillin, (1944) 13
 potassium permanganate, (1944) 13
 prophylactic treatment of wounds, in, (1940) 10
 recent work on, (1944) 13
 sulphonamides, (1941-2) 114 (1944) 13
 urinary, sulphonamides as, (1940) 457, (1941-2) 117
 wounds treated with (1944) 270
- Antiserum**, pneumococcal meningitis treated with sulphonamides and, (1941-2) 304
- Antispasmodics**
 benzyl- α -dimethylamino- β -phenyl- γ -ethylpropionate hydrochloride as, (1941-2) 333
 traserutin, in gastro-intestinal disorders, (1940) 462
- Antistreptolysin titres** in rheumatic fever, (1940) 511
- Antitoxin**
 botulism treated with, (1941-2) 173
 bovine, in prophylaxis of tetanus, (1943) 361
 diphtheria, (1941-2) 209, 260, (1943) 56, 190
 scarlet fever, prophylaxis of, (1940) 514
 tetanus, (1941-2) 407
- Antityphoid serum**, value of, (1939) 17
- Antium**, spontaneous haemorrhage into, (1939) 334
- Antipol**, trypanosomiasis treated with, (1944) 391
- Antutrin-S**
 skin test in pregnancy, (1939) 489, (1941-2) 357
 undescended testis, in, (1940) 551
- Anuria**
 bismuth causing, (1941-2) 410
 cholera complicated by, (1943) 174
 crush syndrome, in, (1944) 271
 potassium salts and, (1941-2) 408
 sulphadiazine causing, (1943) 304, (1944) 328
 sulphapyridine calculi causing, (1941-2) 161
 sulphapyridine causing, (1944) 278
 sulphonamide therapy causing, (1941-2) 346, (1944) 396
- Anus**
 carcinoma, squamous-celled, (1941-2) 147
 diseases, (1939) 220, (1941-2) 147
 faecal soiling of perianal skin, (1941-2) 147
 haemorrhoids, Arnheim's technique for removal of, (1939) 220
 pruritus ani, fungi causing, (1939) 221
 tuberculous, (1943) 128
- Anxiety neurosis**
 cardiac disease, association with, (1944) 341

CUMULATIVE INDEX

Anxiety states

- convulsion therapy, (1941-2) 80
- glaucoma, aetiological factor in, (1940) 313
- hyperventilation in, (1940) 485

Aorta

- abdominal, embolus of, (1943) 125
- occlusion of, (1941-2) 153
- thrombosis, (1940) 195
- aneurysm of, (1939) 213 *See also* Aneurysm, aortic
- kymography, (1939) 213
- treatment, (1939) 213
- coarctation,
 - fatal rupture of aorta, (1944) 248
 - occurrence of adult type in children, (1944) 151

- diameter, in status lymphaticus, (1944) 383
- elasticity, changes with age, (1940) 196
- right-sided, (1941-2) 246
- rupture, coarctation, in, (1944) 248
- syphilitic lesions of, (1941 2) 249
- thoracic, rupture of, (1943) 122

Aortic

- aneurysm *See* Aneurysm, aortic
- arch, right-sided, (1941 2) 246
- regurgitation, (1943) 239
- Austin Flint's presystolic murmur in, (1943) 239
- diagnosis, (1943) 239
- syphilitic endocarditis in, (1941 2) 249
- valve,
 - diseases, syphilis and acute rheumatism causing, (1943) 238
 - insufficiency, systolic pressure in extremities in, (1941 2) 252
 - syphilitic lesions, (1943) 238

Aortic, syphilitic, (1943) 134

Aperients, abuse of, (1944) 190

Aphonia, functional, (1944) 283

Apicitis, (1943) 199

Apicolysis

- paraffin-pack, (1940) 392
- pulmonary tuberculosis, in, (1940) 392

Aplastic anaemia *See also* Anaemia, aplastic

- aetiology and pathology, (1939) 206
- spinal puncture in, (1939) 248

Apnoea neonatorum (1941 2) 156

Aponeurotic transplantation, head injury, in, (1940) 348

Apophysitis, acromion, of, (1940) 296

Apoplexy

- air embolism causing, (1943) 128
- carotid sinus stimulation causing, (1943) 129
- prognosis, (1940) 189
- utero-placental, (1944) 24

Appendicitis, (1939) 221, (1941 2) 148 (1944) 145

- acute,
 - age incidence, (1944) 145
 - analytical observations, (1944) 146
 - bradycardia in, (1943) 130
 - clinical picture, (1944) 146
 - anomalies, (1944) 146
 - closed loop intestinal obstruction, (1944) 146
 - complications, (1941 2) 148
 - conditions simulating, (1941 2) 125, (1944) 119
 - differential diagnosis, (1944) 119
 - mortality, (1941 2) 149
 - old age, in, (1941 2) 148
 - osyutidias causing, (1943) 129
 - persons over fifty, in, (1944) 145
 - post-operative acute hepatitis, jaundice and bleeding, (1941 2) 149
 - prognosis, (1941 2) 149
 - rheumatic fever associated with, (1941 2) 377
 - symptoms, evaluation of, (1944) 119
 - treatment,
 - ambulatory, (1941 2) 148
 - children, in, (1943) 130, (1944) 147
 - health education, value of, (1944) 147
 - youth and old age, in, (1943) 129
- aetiology, (1940) 189
- chronic, (1943) 130
- clinical picture, (1941-2) 149
- diagnosis, (1944) 147
- ileo-gastric syndrome and, (1944) 147

Appendicitis—*continued*

- complications, (1940) 12
 - diagnosis, (1944) 148
 - differential diagnosis,
 - ovulation, pain due to, (1940) 190
 - pneumothorax therapy, during, (1940) 391
 - drainage after, (1940) 190
 - early treatment of, (1940) 12
 - Enterobius (oxyuris) vermicularis*, presence of, (1941-2) 149, (1944) 145
 - leucocyte count in, (1939) 221
 - mortality, (1940) 12
 - neurogenic, (1940) 189, (1943) 130
 - old age, in, (1940) 191
 - pain in, (1940) 141
 - pathology, (1944) 145
 - peritonitis,
 - sulphanilamide in, (1940) 190
 - treatment of, (1939) 222
 - retrocaecal, diagnosis and surgical approach, (1943) 130
 - spinal, (1941 2) 125
 - sulphanilamide in, (1940) 190
 - treatment, (1939) 221, (1940) 190, (1944) 148
 - tumours of appendix, (1939) 222
- ## Appendicostomy, ulcerative colitis, in, (1940) 27
- ## Appendix
- adenocarcinoma with metastases, (1944) 148
 - carcinoid tumour, (1944) 148
 - epiploica, torsion of, (1941-2) 125
 - oxyuris vermicularis in, (1941-2) 149
 - sensitiveness of, (1940) 141
 - stump, healing of, (1940) 190
 - tumours, (1939) 222 (1944) 148
- ## Apple diet
- diarrhoea, in, (1940) 269
 - infant diet, in, (1939) 382
 - lead poisoning, in, (1940) 378
- ## Apraxia, limb kinetic, ideokinetic and ideational, (1944) 149
- ## Aqueous humour, concentration of sulphonamides in, (1941-2) 342
- ## Arachis oil, substitute for olive oil, (1940) 127
- ## Arachnodactyly, (1940) 301
- associated stigmata and aetiology, (1943) 159
 - case in a Chinese, (1943) 160
 - typical case of, (1939) 253
- ## Arachnoiditis, (1939) 322
- spinal, (1939) 544
- ## Arcus senilis, aetiology of, (1939) 293
- ## Ardea, (1939) 471
- ## Arflexia, tendinous, (1940) 507
- ## Argentaffine cells, pernicious anaemia, and, (1940) 168
- ## Argyll Robertson pupil, pseudo, (1939) 222, (1944) 149
- ## Argyria, nasal medication causing, (1940) 235
- ## Argyrol, displacement therapy in suppuration of middle ear, (1940) 284
- ## Arhinencephaly, (1940) 408
- ## Arthralgias, ocular manifestations, (1940) 587
- ## Arm
- endometriosis of, (1939) 329
 - lymphoedema of, (1940) 397
 - oedema, hysterical, of hand and, (1940) 426
 - sympathetic denervation of, (1944) 81
- ## Armour, protective, in warfare, (1940) 11
- ## Army *See also* Aviation and War
- morale in, (1944) 342
 - psychoneuroses in, (1944) 340 5
 - pulmonary tuberculosis in, (1943) 61
- ## Arrhenoblastoma, ovary, of, (1943) 294
- ## Arrhythmia, (1939) 223, (1940) 191-3, 317, (1941 2) 149, (1943) 131
- auricular fibrillation in infancy, treatment of, (1939) 224
 - bradycardia, cardiazol (metrazol) in, (1939) 223
 - paraldehyde in, (1939) 223
 - extrasystole in children, (1939) 223
 - hypertensive heart disease, in, (1940) 193
 - magnesium glutamate in treatment, (1940) 317
 - necrosis of pancreas associated with, (1939) 455
 - quinidine treatment of, (1939) 59

CUMULATIVE INDEX

Arrhythmia—continued

- tachycardia, quinidine in, (1939) 223
- treatment, ouabain in, (1944) 321
- Arsenic
 - anthrax treated with sulphapyridine and, (1943) 128
 - compounds,
 - toxicity, (1941–2) 332
 - trypanosomes, effect on, (1941–2) 332
 - dermatitis, herpes simplex associated with, (1941–1942) 256
 - effect of thiosulphate on excretion of, (1941–2) 404
 - mountain sickness, as prophylactic for, (1939) 280
 - poisoning,
 - cerebral symptoms, (1941–2) 410
 - peripheral neuritis, vitamin B therapy, (1941–2) 410
 - purpura haemorrhagica caused by, (1940) 325
 - syphilis treated with, (1943) 89, 356–8
- Arsenical
 - compounds, syphilis treated with, (1941–2) 404
 - encephalitis, (1944) 25
- Arsenoxide, syphilis, in, (1940) 87, (1941–2) 105
- Arsphenamine
 - dermatitis, (1941–2) 332
 - encephalopathy caused by, (1941–2) 332
 - haemorrhagic encephalitis caused by, (1944) 221
 - harmful effects of, (1941–2) 332
 - jaundice caused by, (1941–2) 332, (1944) 35
 - keratoderma blennorrhagica, in, (1939) 155
 - myocarditis, acute interstitial, caused by, (1941–2) 332
 - poisoning, (1940) 549
 - purpura haemorrhagica due to, (1941–2) 213
 - syphilis, in, (1940) 87; (1943) 89, 356–8
 - intravenous drip, (1943) 358
 - massive-dose therapy, (1943) 357
 - results, (1943) 357
 - side-effects, (1943) 358
- Arterial
 - arteritis, chronic, (1939) 225
 - circulation,
 - action of vasodilator drugs, (1941–2) 151
 - devascularization of stomach, experimental, (1944) 150
 - method of increasing arterial flow to an extremity, (1941–2) 151
 - plethysmographic method of measuring peripheral flow, (1941–2) 151
 - disease and degeneration, (1939) 224
 - occlusion, peripheral, (1944) 82
 - periarteritis nodosa, (1939) 224
 - spasm, traumatic, (1944) 83
 - thrombo-angitis obliterans, (1939) 224
- Arteries
 - ageing of, (1941–2) 151
 - diseases, (1940) 193–7, (1941–2) 150, (1943) 131, (1944) 150
 - occlusive, (1940) 194
 - embolic, acute, (1944) 83
 - peripheral, pancreatic extract in treatment, (1944) 324
 - spasm, traumatic, (1944) 83
- Arteriography, (1940) 103
- cerebral, (1940) 103
- Arteriosclerosis, (1943) 133
- cerebral, (1943) 134
- glomerulo-nephritis and, (1944) 311
- infantile, (1941–2) 152
- intercapillary glomerulo-sclerosis and, (1941–2) 152
- mental disorders, relation to, (1943) 134
- obliterans, (1943) 133
- Arteriosclerotic
 - endarteritis, sympathectomy for, (1944) 151
 - muscular rigidity, (1944) 166
 - Parkinsonism, (1944) 166
- Arteriovenous fistula
 - congenital, (1940) 301
 - diagnosis of, (1941–2) 421
 - treatment, (1941–2) 422
- Arteritis
 - chronic, (1941–2) 151; (1943) 133, (1944) 151
 - pathology, changes in elasticity of aorta with age, (1940) 196
 - temporal, (1941–2) 152; (1943) 131

- Artery, splenic, aneurysm of, (1941–2) 398
- Arthralgia, cobra venom in treatment of, (1940) 300
- Arthritis, (1939) 226; (1941–2) 153, (1944) 151–4
- acute infective, *Bacillus supestifer* infection in, (1943) 135
- alopecia of peroneal region in, (1940) 165
- band-shaped keratitis associated with, (1943) 180
- chronic,
 - adults, in, (1944) 152
 - infective, cervicitis causing, (1939) 228
 - serum phosphatase in, (1940) 201
- coccidioidal, (1943) 146
- foreign bodies in joints causing, (1940) 360
- gonococcal, (1939) 226 *See also* Gonococcal arthritis
- keratosis blennorrhagica, and, (1943) 136
- menopausal *See* Menopausal arthritis
- osteoarthritis, (1939) 228
- palindromic rheumatism and, (1943) 122
- rheumatoid, (1939) 226 *See also* Rheumatoid arthritis
- unsolved problem of, (1940) 7
- Still's disease, aetiology of, (1939) 230
- suppurative, (1943) 135
- sulphanilamide in, (1940) 197
- treatment, (1939) 229
- autohaemotherapy and artificial fever, (1940) 201
- cobra venom, (1940) 300
- colloidal iodized sulphur, (1940) 200
- gold therapy, (1940) 7
- oestrogenic therapy, (1940) 201
- vitamin C and sanocrysin, (1940) 200
- Arthropods, disease, relation to, (1944) 154
- Arthrosis, angioneural, (1943) 112
- Articular cartilage, radiography, (1940) 102
- Artificial fever therapy *See* Pyretotherapy
- Artificial respiration, indications for prone pressure method, (1941–2) 212
- Ascariasis, necrosis of pancreas caused by, (1939) 455
- transmission across placenta examined, (1939) 230
- treatment by phenothiazine, (1941–2) 156
- Aschheim-Zondek test, modification of, (1940) 478
- Aschoff nodes, pathology of, (1939) 138
- Ascites,
 - aetiology of, (1939) 230
 - foetal, obstructed labour due to, (1941–2) 279
 - hepatic cirrhosis and, associated with hernia, (1941–2) 255
- Ascoli's treatment of splenomegaly, (1941–2) 398
- Ascorbic acid *See also* Vitamin C
- blood, estimation in, (1940) 116
- content of blood in asthma, (1941–2) 157
- dermatitis gangrenosa infantum in, (1939) 300
- pre-operative preparation, in, (1939) 24
- diabetes mellitus treated with, (1941–2) 206
- dosage, (1940) 130
- gingivitis treated with, (1941–2) 308
- glomerulo-nephritis treated with, (1940) 422
- hepatic function, influence on, (1940) 587
- intravenous injections, in corneal conditions, (1941–2) 198
- plasma, in, (1940) 116
- red blood corpuscles, in, (1940) 116
- tuberculosis, pulmonary, in, (1940) 390
- Asphyxia
 - children, in, (1939) 231, (1941–2) 156
 - new-born, in, (1941–2) 156, (1943) 138
 - causes, (1941–2) 156
 - resistance to asphyxia, (1939) 231
 - treatment, (1941–2) 156
 - helium-oxygen mixture, (1941–2) 156
 - oxygen, (1941–2) 156
- Asphyxiant gases, (1940) 310
- Aspiration
 - biopsy of the liver, (1940) 28
 - joint effusions, of, (1940) 200
- Aspiration pneumonia, (1943) 166
- Aspirin
 - gastric mucosa, effect on, (1939) 48
 - haematemesis due to, (1940) 322

CUMULATIVE INDEX

Asthenia, neurocirculatory. *See* Effort syndrome

Asthenopia, vitamin A therapy, (1940) 202

Asthma, (1939) 200, 231, (1941-2) 157

adrenaline, (1939) 233

aetiology, (1940) 202; (1941-2) 157

aminophylline, (1939) 233

ascorbic acid, relation to, (1941-2) 157

bilharziasis complicated by, (1939) 240

bronchial,

carcinoma complicating, (1943) 138

sulphonamide compounds in, (1943) 138

bronchostenosis complicating, (1941-2) 157

clinical picture, (1940) 203, (1941-2) 157

complications, (1943) 138

cyclopropane anaesthesia, (1939) 234

eosinophil counts in, (1939) 231

gum acacia causing, (1941-2) 157

morbid anatomy, (1941-2) 158

periarteritis nodosa and, (1940) 202

prophylaxis of attacks of, (1940) 203, (1943)

138

psychic factors, (1944) 154

pulmonary eosinophilia and, (1941-2) 157

radiography, (1939) 231

relation to infections of upper respiratory tract,

(1941-2) 157

specific sensitization, (1941-2) 157

status asthmaticus, (1941-2) 158

treatment, (1941-2) 158

acetyl- β -methylcholine, (1941-2) 333

adrenaline (and in oil), (1939) 233, (1940) 203

aminophylline, (1939) 233, (1940) 203, (1941-2)

158

broncho-dilator solutions, continuous inhalation of, (1940) 203

choline derivatives, (1941-2) 333

helium and oxygen, (1939) 234

insulin shock, (1939) 232

lumbar puncture, (1939) 233

neosynephrine, (1940) 203

nicotinic acid, (1944) 155

perisymphatic injections, (1941-2) 158

pyrexia, artificial, (1940) 161

ragweed pollen in, (1939) 200

resection of posterior pulmonary plexus, (1939)

232

short-wave therapy with rotating electrode,

(1939) 233

'slow' adrenaline, (1940) 204

sulphonamides, in, (1943) 138

theophylline ethylene diamine in, (1943) 2

mono-ethanolamine, (1941-2) 158

wide-field X-ray therapy, (1940) 105

types in adults, (1941-2) 157

vitamin C, increased demand for, (1941-2) 157

A T 10 *See* Dihydrocholesterol, *also* Vitamin D

Ataxy, Leyden-Westphal's acute, (1939) 234

Atabrin

flagellate infection, in, (1940) 269

gastrointestinal infection, in, (1940) 269, (1941-2) 24

malaria, in treatment of, (1939) 144, 423, (1940)

76, (1943) 82, 277, (1944) 97

mepacrine hydrochloride, official name for, (1940)

127

relation of toxic manifestations to dosage, (1939)

471

Atabrin musonate, mepacrine methanesulphonate,

official name for, (1940) 127

Atelectasis, (1940) 388

aetiology, (1941-2) 290

allergy, role of, (1940) 388

children, in, (1940) 388

massive, in new-born, (1941-2) 290

post-operative, bronchoscopy in, (1940) 388

Athetosis, double or bilateral, (1941-2) 159

Athletes

circulation in, (1940) 204

collapse, acute fatal non-traumatic, in, (1940)

205

heart of, (1940) 204

injuries of, (1940) 205

knee injuries, (1940) 205

Athlete's foot, infectivity and prevention of, (1939)

343

Athletic injuries, (1941-2) 159; (1943) 139

Athletics, (1940) 204

athletic injuries, and, (1939) 235

crepitating peritendinitis, immobilization treat-

ment of, (1939) 235

sprains, procaine infiltration of, (1939) 235

trochanter minor, isolated rupture of, (1939) 235

urine prior to and after race, (1939) 235

Atmospheric pressure

Eustachian tube, effect on, (1940) 48

low,

whooping cough, effect on, (1944) 408

Atopic dermatoses, histamine treatment of, (1943)

112

Atresia

duodenal, (1941-2) 272, (1943) 253; (1944) 233

oesophageal, (1940) 427, (1941-2) 318

Atrophy

generalized, (1944) 367

joints, of, post-traumatic, (1940) 361

optic, tryparsamide therapy in, (1941-2) 162

Atropine

dangers of, (1944) 232

duodenal ulcer, in treatment of, (1939) 47

poisoning, (1940) 556, (1941-2) 409

pupil, effect on, (1940) 449

scorpion toxin, antidote to, (1940) 448

spasm, in, (1939) 165

sulphate, retinitis pigmentosa treated by, (1941-

1942) 376

Atropine-adrenaline-strophanthin mixture, resusci-

tation, use in, (1940) 509

Atropine methylnitrate (eumydrin) in congenital

pyloric stenosis, (1939) 165 *See also*

Eumydrin

Audiometric tests, of aviators, (1941-2) 160

Auditory acuity, effect of aircraft noise on, (1941-2)

36

Auditory meatus, external, injuries, (1940) 46

Aural

haemorrhage, caused by aneurysm of internal

carotid, (1941-2) 144

infections, sulphonamides in, (1941-2) 118

vertigo, (1939) 88, (1941-2) 422

Auramine, staining of tubercle bacilli by, (1943) 368

Auricles for slightly deaf, (1939) 100

Auricular

aneurysm, (1939) 214

fibrillation,

aetiology, (1941-2) 150

digitalis in, (1940) 192

standstill, (1940) 192

Auscultation

abdomen in intestinal obstruction, of, (1943) 102

heart, of, (1941-2) 245

Austin Flint murmur, (1943) 239

Auto-agglutination, due to cold, in Raynaud's

phenomenon, (1943) 325

Autohaemotherapy

arthritis, in, (1940) 201

menorrhagia, in, (1939) 430

urticaria, in, (1939) 200

Autonomic nervous system

hypogastric plexus, (1944) 83

intra-abdominal lesions and, (1944) 85

'mega' syndromes, (1944) 85

peripheral vascular disturbances, (1944) 81

recent work on, (1944) 81

Autotopnosia, hemiplegia, in, (1943) 241

Avartin, (1939) 163

anaesthesia, (1941-2) 142, (1943) 121

benzedrine for interrupting anaesthesia, (1940) 177

bromethol, official name for, (1940) 127

ureteral calculus treated with, (1941-2) 276

Aviation, (1939) 236, (1941-2) 159, (1944) 155 *See*

also Flying

acero-otitis media in, (1941-2) 182

air embolism, (1943) 6, 140

air-sickness, (1941-2) 36

amaurosis fugax, (1940) 206

anoxaemia, problems of, (1943) 140

audiometric tests in, (1941-2) 160

bibliography of, (1944) 155

'black-out', (1939) 236, (1940) 206, (1941-2) 33

bodily adjustments in, (1944) 155

cardiovascular stability, (1941-2) 30

CUMULATIVE INDEX

Aviation -continued

- cardiovascular tests in, (1943) 140
 - cold, protection against, (1941-2) 35
 - diseases associated with, (1939) 238
 - ear in relation to, (1940) 48
 - effect of altitude changes on intracranial volume, (1941-2) 160
 - effects of flying, (1944) 156
 - Eustachian tube, physiology of, (1940) 48
 - fatigue in, (1941-2) 35, (1943) 6, 141
 - flying aptitude, (1941-2) 29
 - glare, protection against, (1941-2) 36
 - hearing, effect of noise on, (1940) 206, (1941-2) 36
 - effect of flight on, (1941-2) 160, (1943) 141, 182
 - high-altitude flying, (1941-2) 30
 - hyperventilation in, (1941-2) 159, (1943) 140
 - hypotension in relation to, (1939) 236
 - intra-ocular pressure at high altitudes, (1941-2) 160
 - labyrinthine apparatus and, (1940) 205
 - maintenance of physiological efficiency of flying men, (1941-2) 32
 - medicine, (1941-2) 29
 - nervous energy reserve and exhaustion, (1943) 141
 - night-vision, (1941-2) 30, 36
 - oxygen want, (1941-2) 32, (1943) 6, 139
 - parachute descents, (1941-2) 33
 - peptic ulcer in, (1941-2) 160
 - physiology of, (1944) 155
 - pilots, examination of, (1940) 205, (1943) 140
 - psychological pre-selection of flying men, (1941-2) 32
 - special senses, examination of, (1941-2) 160
 - stereoscopic vision, (1941-2) 31
 - visual problems, (1941-2) 36
 - visual requirements for night-flying, (1939) 238
- Vitaminosis** *See* Vitamins, deficiency
- Avoileum**, (1941-2) 327 *See also* Vitamin A
- Axerophthol**, (1940) 128 *See also* Vitamin A
- Axillary veins**, thrombosis of, (1941-2) 420
- Ayerra's disease** *See* Ascites
- Azo-arsenobenzene**, trypanosomiasis treated with, (1944) 100
- Azoman**, (1941-2) 79 *See also* Cardiazol
- Azoospermia**, gonadotrophic hormone in, (1939) 158
- Azosulphamide**
 - anticonvulsive action of, (1943) 203
 - epilepsy treated by, (1943) 203

B

- β -erythroidine hydrochloride, encephalitis epidemica treated with, (1941-2) 332
- β -methylcholine urethane, in treatment of urinary retention, (1941-2) 161
- Babinski's sign**, interpretation of, (1941-2) 376
- Bacilluria**
 - renal tuberculosis, in, (1940) 365
- Bacillus**
 - aerogenes*, eating utensils contaminated by, (1944) 42
 - aertrycke*, food poisoning caused by, (1944) 235
 - paraperitussis*, respiratory infection due to, (1943) 180
 - proteus*, wounds infected by, (1941-2) 267
 - supstifer* infection, suppurative periarthritis due to, (1943) 135
 - tuberculosis*, effect of anthracite dust on, (1941-2) 415
 - sulphapyridine, effect of, (1941-2) 415
 - unsuspected carriers of, (1941-2) 414
- Backache**, (1941-2) 161
 - extrinsic causes, (1943) 142
 - intrinsic causes, (1943) 142
 - low, (1940) 515, (1943) 331, (1944) 362
 - lumbago, and, (1939) 238
 - novocain therapy for ischialgia, (1939) 239
 - posture and occupation in relation to, (1939) 238
 - protruded intervertebral disks as cause of, (1940) 6
 - radiological diagnosis, (1943) 142
 - sacralization of fifth lumbar vertebra, (1940) 207
 - stimulating visceral disease, (1943) 142
 - treatment by immobilization, (1943) 142

Bacteria

- eating utensils contaminated by, (1944) 42
- spore-forming, in milk, (1941-2) 232
- Bacteriæmia**, (1944) 367-9
 - eye diseases and infections, in, (1944) 367
 - staphylococcal,
 - penicillin in, (1944) 368
 - sulphathiazole in, (1943) 332
- Bacterial allergens**, sensitization to, in dermatitis herpetiformis, (1941-2) 204
- Bactericidal action**
 - aerosols, (1943) 53
 - gramicidin, of, (1943) 308
 - ultra-violet light, of, (1943) 53
- Bacteriology**
 - advances in, (1939) 13, (1944) 37
- Bacteriophage**
 - staphylococcal septicaemia, in, (1940) 519
 - Vi, in typing of typhoid bacilli, (1944) 222
 - Bacteriostatic effects of penicillin, (1943) 302
- Bacteriostatic values** of acriflavine and proflavine, (1941-2) 330
- Bacterium**
 - coli*,
 - sulphanilamide, action on, (1940) 133
 - urinary tract infection, sulphanilamide in, (1940) 208
 - enteridis*, infection, complicating cerebrospinal fever, (1941-2) 186
 - monocytogenes*, in relation to glandular fever, (1941-2) 235
 - tulænce*, culture of, (1943) 368
 - intracellular parasitism and, (1941-2) 415
 - typhosum*, new types of organism, (1944) 37
- Bagassosis**, (1944) 372
- Balanitidum coli** infection, amoebiasis associated with, (1940) 167
- Balneo-therapy**, nerve lesions, in, (1943) 244
- Banana**
 - diet, in colic disease, (1939) 283
 - for infants, (1939) 382
 - diet of children, in, (1941-2) 262
 - dietary supplement, as, (1940) 270
 - maintenance of nutrition in typhoid fever, for, (1941-2) 221
 - preparations, infantile diarrhoea treated with, (1941-2) 209
- Bandage**
 - elastic adhesive, in thrombo-phlebitis, (1940) 582
 - transparent, (1940) 350
- Banti's syndrome**
 - ætiology, (1941-2) 398
 - splenectomy in, (1941-2) 398
- Bantus**, multinucleosis among, (1941-2) 416
- Barberry root**, antiseptic properties of, (1941-2) 332
- Barbiturates**, (1939) 17, 163
 - gastric secretion, effect on, (1940) 557
 - poisoning, (1939) 569, (1940) 557-9, (1941-2) 409
 - antidotes, (1941-2) 409
 - benzedrine by intravenous drip, (1941-2) 346
 - cardiazol in treatment of, (1940) 558
 - picROTOXIN in treatment of, (1940) 558
 - sedatives, as, (1941-2) 332
 - short-acting, (1943) 121
 - sulphapyridine, use with, (1940) 472
 - toxic effects of, (1939) 211
- Barium sulphate**, meal, perforation of duodenal ulcer following, (1940) 438
- Bar-tenders**, occupational dermatitis in, (1940) 259
- Basal**
 - ganglia, functions of, (1941-2) 90
 - metabolism in nephrosis, (1939) 443
 - narcosis, (1940) 177, (1941-2) 142, (1943) 121
 - contra-indications and uses, (1944) 136
 - pentothal sodium, (1944) 137
- Baseball pitcher**, injuries of, (1943) 139
- Bayer 205**, (1941-2) 112
 - suramin, official name for, (1940) 127
 - trypanosomiasis, in, (1939) 146; (1943) 367
- Beal's type** of acute follicular conjunctivitis, (1944) 187
- Beau's lines**, (1944) 308
- Bed**, oscillating, occlusive arterial disease treated by, (1940) 194

CUMULATIVE INDEX

Bee
 stings, hypersensitiveness to, (1940) 160
 venom, rheumatoid arthritis treated with, (1940) 198, (1941-2) 155

Beethoven's deafness, (1941-2) 56

Belladonna
Bulgarian,
 paralysis agitans treated with, (1939) 458
 post-encephalitic Parkinsonism, in, (1939) 327
 duodenal or pyloric spasm, in, (1939) 167
 phenobarbitone, and, epilepsy treated by, (1941-1942) 222

Benerva, vitamin B₁ preparation, (1940) 129

Benzedrine, (1939) 164, (1943) 93
alcoholism, in treatment of, (1939) 197
 avertin anaesthesia interrupted by, (1940) 177
 blood pressure, effect on, (1939) 249
 cardiovascular system, effect on, (1940) 449
 cerebral circulation, effect on, (1940) 56
 circulation, effects of inhalation on, (1940) 449
 effects of large doses for long periods, (1940) 449
 heart disease, effects of inhalation in, (1940) 449
 intravenous drip administration, (1941-2) 346
 metabolism, effect on, (1940) 449
 obesity, in, (1940) 152
 Parkinsonism treated with, (1940) 287
 pressor effect, (1940) 450
 sodium amytal anaesthesia, effect on, (1940) 178
 sulphate, (1943) 93
 dysmenorrhoea treated with, (1941-2) 214
 gastric and intestinal acidity, effect on, (1939) 472
 obesity in children, in, (1941-2) 130

Benzedrine-homatropine cycloplegia, (1940) 508

Benzene poisoning, (1940) 560 2, (1941-2) 411, (1944) 387
 blood picture in, (1940) 561
 chronic, diagnosis of, (1941-2) 411
 industrial aspects, (1940) 561
 pathology, (1940) 561
 printers, in, (1941-2) 411

Benzocaine, pain, in treatment of, (1939) 454

Benzochrome in cystitis, (1939) 243

Benzol. *See* Benzene

Benzyl- β -dimethylamino- α -phenyl- α -ethylproprionate hydrochloride
 antispasmodic action of, (1941-2) 333
 compared with papaverine, (1941-2) 333

Benzyl benzoate, (1941-2) 112
 scabies treated with, (1941-2) 391 (1943) 342, (1944) 117, 372

Benzylmethylcarbamine, (1943) 93

Benzylsulphanilamide, (1940) 133

Berberine sulphate, oriental sore, in, (1940) 136

Berberis trifoliata, antiseptic properties of, (1941-2) 332

Berr-beri, (1939) 239, (1941-2) 26
 alcoholic, and vitamin B deficiency, (1941-2) 135
 aneurin cure of symptoms of, (1939) 18
 heart, (1941-2) 5
 infantile, (1943) 143
 skin lesions associated with, (1939) 240
 vitamin B₁ in, (1940) 129
 deficiency following hernia causing, (1939) 149, 239

Weinick's disease and, in pigeons, (1940) 70

Berin, vitamin B₁ preparation, (1940) 129

Besnier-Boeck-Schaumann disease, (1943) 347

Betaxan, vitamin B₁ preparation, (1940) 129

Bier's Congestion, chilblains treated by, (1944) 179

Bile-duct, (1941-2) 233
 biliary papilla and ampulla of Vater, diseases around, (1944) 241
 carcinoma, (1941-2) 234, (1944) 241
 common,
 benign stricture of, (1940) 307
 carcinoma, congenital absence of gall-bladder associated with, (1940) 305
fasciola hepatica removed from, (1941-2) 230
 non-traumatic rupture of, (1941-2) 234
 pathological physiology, (1944) 241
 peristalsis of, (1943) 219
 sphincter mechanism, (1944) 241
 stone in, (1943) 219

Bile-duct—continued
 congenital obliteration, (1941-2) 231
 surgical treatment of, (1940) 14
 diseases, (1940) 305-8; (1941-2) 234, (1943) 219, (1944) 241
 pain, left-sided, in, (1943) 219
 intrahepatic, carcinoma of, (1944) 290
 obstruction, (1940) 307
 operative injury to, (1940) 13
 tuberculosis, (1940) 305

Bilharziasis, (1939) 240
 asthma associated with, (1939) 240
 morbid anatomy, (1940) 207
 treatment, (1939) 240
 testis, of, (1941-2) 405
 vesical, intravenous therapy, (1943) 143

Biliary
 cirrhosis, xanthomatous, (1941-2) 287
 colic, pneumonia complicating, (1943) 219
 diseases, (1940) 6
 drainage, gall-bladder disorders, in diagnosis of, (1939) 48
 dyskinesia, X-ray appearance in, (1941-2) 233
 function, disturbance of, associated with diabetes mellitus, (1940) 263
 tract, surgery of the, (1940) 13

Bilirubin
 excretion test, (1940) 116
 serum, in pernicious anaemia, (1939) 203

Bilirubinemia, limits of normal, (1939) 52

Bilroth I method of gastrectomy, (1940) 13

Biochemical
 changes in mental disease, (1939) 116
 tests in surgery, (1939) 24

Biopsy
 aspiration, of the liver, (1940) 28
 testicular, male infertility, in, (1943) 352

Birth
 incidence of day and night, (1940) 371
 phases of, (1943) 15

Birth-marks
 Grenz-ray therapy in, (1940) 187
 radium therapy, (1941-2) 373

Birth palsies, aetiology and treatment of peripheral, (1939) 240

Bismarsen, lupus erythematosus treated by, (1943) 273

Bismuth
 anuria in infants caused by, (1941-2) 410
 cervico-vaginitis due to, (1940) 550
 elimination of tissue deposits by ammonium chloride, (1941-2) 404
 lead poisoning after use of, (1940) 377
 slow intravenous drip administration, (1943) 301
 toxicity and retention in tissues, (1943) 301

Bistovol as adjuvant in malarial therapy, (1943) 292

Bisulphate binding substances (B B S), blood, in, (1940) 114

Bites
 human, treatment of, (1941-2) 269

Bites and stings, (1943) 143
 scorpion stings, (1939) 241, (1941-2) 161
 snake bites, antivenenes for, (1939) 242
 tick, paralysis caused by, (1939) 241

Bituminous coal, silicosis in miners of, (1941-2) 389

Black hairy tongue, (1941-2) 308

Blacking-out, in aviators. *See* Aviation, 'black-out'

Blackwater fever
 haemolytic process in, (1943) 84
 malaria complicated by, (1943) 83
 treatment of, (1939) 242
 by tincture of *virex peduncularis*, (1943) 144

Bladder
 bilharziasis, intravenous therapy, (1943) 143
 calculi, sulphapyridine, (1941-2) 161
 carcinoma,
 papillary, in diverticulum, (1943) 145
 radiological treatment of, (1939) 242, (1943) 144
 diseases, (1939) 242, (1941-2) 161, (1944) 156
 cystitis, treatment of, (1939) 243
 malignant, (1939) 28
 stone, mortality from operations on, (1939) 243
 tuberculous cystitis end-results, (1939) 244

CUMULATIVE INDEX

Bladder—continued

- diverticulum,
 - malignant papilloma in, (1943) 145
 - operation and use of sodium chloride in, (1944) 156
- faeces, effect of, in, (1941-2) 25
- foreign bodies, (1941-2) 161
- Hodgkin's disease in, (1941-2) 258
- Hunner's ulcer, (1944) 94
- cystoscopy in, (1944) 94
- treatment, (1944) 95
- irritable, due to cervicitis, (1941-2) 21
- mucosa, bony gaps filled with, (1939) 260
- nervous diseases, (1941-2) 161
- papillomatosis, treatment with disinfectants, (1944) 156
- tuberculosis, advanced, treatment, (1944) 95
- urethral catheter in, (1941-2) 161
- urinary,
 - diseases, (1940) 207-9
 - ectopia of, surgical treatment, (1940) 14
 - lichen planus of, (1940) 207
 - neuralgia, (1940) 207
 - 'tabetic cord', (1940) 425
 - tumours, malignant, treatment, X-rays, super-voltage, (1940) 208

Blast

- ear, effects on, (1940) 47
- injuries, (1940) 9, (1941-2) 3, 10, 73, 297; (1943) 251
 - chest complications, (1941-2) 297
 - clinical picture, (1941-2) 74
 - effect on lungs, (1941-2) 297
 - experimental investigations, (1941-2) 298
 - lung, of, (1943) 271, (1944) 273
 - pathology, (1941-2) 73
 - phrenico-costal sinus pneumonia, (1941-2) 298
 - treatment, (1941-2) 74
 - tympenic membrane ruptured by, (1940) 47
- mental symptoms as result of, (1944) 79
- neurological effects of, (1941-2) 90
- psychiatric syndromes and, (1943) 251

Blastomyces gilchristi, (1940) 209

Blastomycosis, (1943) 145, (1944) 157

disseminated, (1940) 209

Fallopian (uterine) tube, of, (1939) 339

Bleeding time, determination of, (1939) 53, (1940) 210, 211

Blepharitis, treatment, (1944) 232

brilliant green, (1941-2) 227

gentian violet and brilliant green paste, (1941-2) 227

Blindness, (1939) 244, (1941-2) 162, (1944) 157

blood diseases causing, (1941-2) 162

causes, (1944) 157

degenerations and optic atrophy causing, (1941-2) 162

haemorrhage causing, (1941-2) 162

incidence, (1944) 157

night, (1941-2) 5, (1943) 80, 206 *See also* Night blindness

vitamin A treatment of, (1939) 245

optic atrophy, tabetic, treatment of, (1939) 244

syphilis causing, (1940) 210

toxic amblyopia, vitamin B₁ treatment of, (1939) 244

treatment, (1943) 146

tumours, (1943) 147

Blood

acidosis, in, (1941-2) 128

agglutination tests, Rh factor, (1943) 148

amino-acids in nephrotic crisis, (1940) 421

bromine content, reduction by thyroid extract, (1941-2) 337

calcium, (1940) 114

carbon dioxide and gastric acidity, (1940) 437

Castle's factor in pernicious anaemia, (1943) 3, 47

changes,

trichiniasis, in, (1943) 366

whooping-cough, in, (1943) 380

cholesterol,

general, pruritus, in, (1944) 337

hypochromic anaemia of pregnancy, in, (1940) 171

level, effect of X-rays on, (1941-2) 372

Blood—continued

coagulation, (1940) 6, 210

heparin, effect of, (1940) 136, 137; (1941-2) 355, (1944) 159

prothrombin and vitamin K in relation to, (1940) 117

vitamin K and, (1940) 131

coagulation time, (1940) 117

disseminated sclerosis, in, (1944) 207

in the new-born, (1940) 16

cold, transfusion of, (1940) 220

convalescent, herpes zoster ophthalmicus treated with, (1941-2) 198

diastase, low, (1941-2) 163

diseases,

advances in knowledge of, (1940) 6

blindness caused by, (1941-2) 162

distinction, faecal urobilin excretion and, (1944) 303

electrolytes and menstrual cycle, (1941-2) 163

examination of, (1941-2) 163

haemagglutination, (1944) 159

haemoglobin,

derivatives, (1944) 159

women and children, in, (1944) 158, 159

histamine variations, in allergic diseases, (1943) 112

injection of husband's, in hyperemesis gravidarum, (1944) 333

inorganic constituents, (1940) 113

lead content in normal, (1940) 377

nail parings, on, medico-legal examination, (1940) 401

oxygen,

capacity, after hexobarbitone soluble, (1941-2) 142

saturation, (1944) 159

parathyroid hormone in, (1943) 298

phosphatase,

arthritis, chronic, in, (1940) 201

values, in prostatic carcinoma, (1944) 337

vitamin D deficiency, in, (1940) 116

physical and chemical changes, (1941-2) 163

plasma,

burns treated with, (1941-2) 180

coagulated, in nerve suture, (1941-2) 264

dried,

haemophilia, in treatment of, (1943) 229

transfusion of, (1940) 217

globulin fractions, (1940) 121

lipids in obstructive jaundice and hepatic disease, (1943) 148

methods of concentration and drying, (1941-2) 169

potassium,

concentration and toxicity, (1940) 219

partition of, (1940) 220

preparation and use of, (1943) 31, 154

preservation and use of, (1943) 155

proteins of, (1940) 121

prothrombin, (1940) 117

reaction with, (1943) 157

storage of, (1941-2) 169

S. pallida, survival of, in frozen, (1944) 102

substitute for whole blood, (1941-2) 169

transfusion of, (1940) 42-4

effect of adrenal cortical extract, (1941-2) 181

shock, in, (1941-2) 387

storage of, (1940) 220

potassium,

muscular diseases, in, (1940) 68

shock, in, (1940) 528

preserved *See* Blood transfusion

pressor substances in, (1940) 5

promin in, (1941-2) 337

prothrombin, effect of vitamin K, (1941-2) 163, 427

Rhesus factor, (1943) 3, 16, 24, 29, 148

racial incidence of, (1944) 159

rheumatic fever, in, (1943) 327

serological tests, (1944) 159

stored, (1943) 27, 31 *See also* Blood transfusion

malaria transmitted by, (1941-2) 301

subcutaneous injection, malaria conveyed by, (1940) 222

CUMULATIVE INDEX

- Blood—continued**
 sugar, acne, in, (1940) 148
 typhus fevers, in, (1940) 570
 varicose ulcer treated by injection of, (1944) 401
 viscosity, heart failure in, (1940) 337
 tuberculosis, in, (1941-2) 414
 vitamin A in, (1940) 585
 vitamins A and C content in surgical patients, (1940) 592
 whole, in prophylaxis of peritonitis, (1940) 443
 X-ray therapy, toxic effects of, (1941-2) 372
- Blood cells, red**
 after transfusion, (1943) 31
 concentrated suspension of, for anaemia, (1941-2) 168
 concentration of, in transfusion, (1943) 27
 diameter in jaundice, (1940) 356
 diffusion of potassium from, (1940) 219
 effects of haemorrhage on, (1943) 147
 pernicious anaemia, in, (1941-2) 139
 sedimentation rate, in malignant disease, (1941-2) 163
 survival after transfusion, (1941-2) 170
 transfusion of, (1940) 44
- Blood chemistry**
 bisulphite binding substances (B B S), (1940) 114
 gastro-intestinal haemorrhage, in, (1941-2) 139
 inorganic constituents, (1940) 113
 magnesium, (1940) 114
 nicotinic acid, (1940) 115
 potassium, (1940) 113
 pyruvic acid, (1940) 114
 shock, in, (1940) 528
 sodium, (1940) 113
 total base concentration, (1940) 113
 vitamin B₁ in, (1940) 115
- Blood count**
 tick-bite fever, in, (1940) 85
 tuberculosis, pulmonary, in, (1944) 292
- Blood donors**
 allergic, (1943) 30
 faints in, (1943) 31
 malarial donors, (1943) 156
- Blood examination, (1939) 245, (1940) 210, (1941-1942) 163, (1944) 158**
 bleeding time, (1940) 210
 blood from cadavers, chemical analysis of, (1939) 247
 cellular changes, methylene blue reaction, (1939) 245
 chemical analysis, (1939) 247
 coagulation, measuring clot retraction, (1939) 245
 oxygen saturation, (1939) 246
 physical and chemical changes, (1941-2) 163
 platelet count, (1940) 211
 serological tests, formol-gel and Takata-Ara reactions, (1939) 246
 serum phosphatase test, (1939) 247
 sternal puncture, (1943) 247
- Blood-forming organs**
 advances in knowledge of, (1940) 6
 diseases of, (1939) 52, (1940) 31-3, (1943) 3, 23
 anaemias, (1939) 53. *See also* Anaemia
 diagnosis, (1939) 54
 haemorrhagic states, (1939) 53
 treatment, (1939) 54
- Blood groups**
 A and B agglutinogens, (1940) 34
 classification, (1940) 34
 cross-agglutination and syphilis test, rapid method, (1940) 210
 cross-matching, (1943) 29
 international classification, (1940) 34
 M and N agglutinogens, (1940) 34
 plasma transfusion, (1940) 43
 stored blood, transfusion of, (1940) 42
 transfusion, and, (1943) 3, 16, 29
- Blood-levels of various constituents of blood, (1939) 21**
- Blood picture**
 benzene poisoning, in, (1940) 561
 glandular fever, in, (1941-2) 235
 syphilis, in, (1941-2) 102
- Blood platelets count**
 heparin, effects of, (1944) 159
 new-born, in, (1940) 211
- Blood pressure, (1940) 211-7, (1941-2) 164; (1943) 148; (1944) 106 *See also* Hypertension; Hypotension**
 adrenal tumours causing rise of, (1943) 150
 adrenaline, changes due to, (1940) 447
 angiotonin, effects of, (1943) 150
 body build, relation to, (1941-2) 166
 cardiazol, effect of, (1940) 492
 erythraemia, in, (1944) 231
 essential hypertension,
 breath-holding test, (1939) 248
 paroxysmal hypertensive attacks, (1939) 248
 renal disease, relation to, (1939) 248
 estimation,
 auscultatory method, (1941-2) 164
 clinical evaluation of, (1943) 149
 influence of doctor on hypertensive patients, (1941-2) 164
 palpation of brachial artery, (1940) 216
 sphygmomanometers, (1943) 149
 gastro-duodenal haemorrhage, in, (1943) 45
 high, (1939) 249
 aetiology, (1939) 249
 benzedrine, effect of, (1939) 249
 irradiation, (1939) 250
 pregnancy, during, (1939) 30
 renal ischaemia and, (1941-2) 2
 sex factor in prognosis of, (1940) 5
 smoking, effect of, (1939) 249
 toxemia of pregnancy, (1941-2) 18
 unsolved problems in aetiology and treatment of, (1940) 5
 high and low, (1939) 248
 hypotension, orthostatic, (1939) 250
 aviation, in relation to, (1939) 236
 benzedrine and paredrine, effect of, (1939) 250
 methods of measuring, (1939) 56
 normal, (1941-2) 45, (1944) 160
 sex hormones, effects of, (1941-2) 382
 shock, in, (1941-2) 1, 40
 spinal anaesthesia, during, (1941-2) 142
 systolic,
 diastolic pressures, and, (1941-2) 167
 functional aortic insufficiency, in, (1941-2) 252
 veritol, effect of, (1940) 463
- Blood sugar in coeliac disease, (1939) 282**
- Blood transfusion**
 accidents,
 air embolism, (1943) 28
 erythroblastosis foetalis and, (1943) 3, 16, 24, 119, 148
 over-rapid transfusion, (1943) 156
 air-raid casualties, for, (1943) 158
 allergy induced by anti-haemorrhagic substances, (1941-2) 170
 anaemia, in, (1939) 54
 ankylostomiasis, in, (1940) 187
 aplastic, (1940) 35
 iron deficiency, (1939) 54
 volume and rate, (1940) 222
 apparatus and procedure, (1941-2) 168, (1943) 154
 blood and plasma transfusions, indications for, (1940) 42
 blood groups in relation to, (1940) 34
 blood substitutes, use of, (1940) 6
 bone marrow, via the, (1943) 155
 cadaver blood, (1940) 38
 citrated blood, (1940) 39
 clots in apparatus, (1941-2) 168
 cold blood, transfusion of, (1940) 220
 concentrated suspension of red cells for anaemia, (1941-2) 168
 conserved blood, (1939) 251
 diluents, effect of, (1940) 219
 diphtheria, malignant, in, (1943) 30
 diseases transmitted by, (1943) 156
 donors,
 allergic, (1943) 30
 cross-agglutination and syphilis test, (1940) 210
 selection of, for drip-transfusion, (1940) 36
 dried blood plasma, (1940) 217

CUMULATIVE INDEX

Blood transfusion—continued

- drip-transfusion, continuous, (1940) 35
- apparatus, (1940) 36-8
- drip flow meter, (1940) 221
- technique, (1940) 36
- erythrocytes, concentration of, (1943) 27
- extra-corporeal circulating haemoglobin, fate of, (1941-2) 170
- fresh and stored blood, relative merits of, (1943) 154
- gastro-duodenal haemorrhage, in, (1943) 45
- gastro-intestinal haemorrhage, in, (1941-2) 169
- gelatin solutions, use of, (1944) 162
- grouping, (1940) 34
- haematemesis, in, (1943) 228
- treated with drip, (1939) 366
- haemoglobin level in, (1940) 36
- haemoglobin solution as blood substitute, (1940) 218
- haemolysis, factors influencing, (1940) 220
- haemorrhage, in, (1940) 222
- heparin as anticoagulant, (1939) 252
- human serum as blood substitute, (1940) 218
- infants, in, (1939) 250
- infections, acute, in, (1940) 222
- intravascular haemolysis, (1943) 156
- large volumes of blood, (1940) 35
- leprosy, in, (1941-2) 283
- malaria,
 - conveyed by subcutaneous injection of blood, (1940) 222
 - transmitted by, (1941-2) 97
 - transmitted in stored blood, (1941-2) 301
- nephrotic syndrome, in, (1943) 31
- new factors in, (1943) 27, 158
- placental blood, (1939) 251, (1940) 30, 221
- plasma, (1940) 11, 42
- burns, in, (1941-2) 180
- dried, (1940) 43, 217
- grouping, (1940) 43
- interchangeability of serum and, (1940) 221
- methods of concentration and drying, (1941-2) 169
- potassium and toxicity, (1940) 219
- preservation and use of, (1943) 155
- reaction with, (1943) 157
- serum, preparation of, (1943) 154
- shock, in, (1941-2) 387
- storage of, (1940) 220 (1941-2) 169
- stored plasma, (1940) 43
- substitute for whole blood, (1941-2) 169
- pooled concentrated human serum, in shock, (1941-2) 388
- preserved blood, (1940) 218
- diluents, effect of, (1940) 219
- haemolysis, factors influencing, (1940) 220
- preservatives, effects of, (1940) 219
- sulphanilamide, use of, (1940) 219
- pump, Riddell's reversible rotatory, (1940) 35
- rate of transfusion, (1940) 35
- reactions after, (1940) 41, 220 (1941-2) 169 (1943) 30, 155
- allergy induced by anti-haemorrhagic substances, (1941-2) 170
- avoidance of, (1943) 28
- fate of extra-corporeal circulating haemoglobin, (1941-2) 170
- pyrexial, (1943) 156, 158
- renal insufficiency, (1941-2) 170
- Rhesus factor, (1943) 3, 16, 24, 29, 148
- stored human blood, (1941-2) 169
- recent developments in, (1940) 34
- red cells,
 - concentrated suspension of, (1941-2) 168
 - sedimented, transfusion of, (1940) 44
- refrigerated blood, device for warming, (1941-2) 168
- renal damage and oliguria, (1943) 30
- renal insufficiency resulting from, (1941-2) 170
- retinal haemorrhage after, (1943) 326
- serum,
 - blood substitute, as, (1940) 218
 - nephrotic syndrome treated with, (1943) 289
 - plasma, and, interchangeability of, (1940) 221

Blood transfusion—continued

- shock, (1941-2) 387
- treatment of, (1941-2) 38
- single transfusion versus continuous drip, (1940) 35
- skin pigmentation produced by ultra-violet irradiation and, (1940) 151
- slow drip, (1940) 35
- soluble protein and blood volume, (1941-2) 168
- solutions, (1943) 27
- statistics of, (1943) 156
- stored blood, (1940) 38
- addition of glucose to, (1943) 15
- administration, (1940) 41
- anticoagulants, (1940) 40
- changes in, (1940) 40, 42
- collecting apparatus, (1940) 39
- depots, (1940) 39
- grouping, (1940) 42
- heparin as anticoagulant, (1940) 137
- malaria transmitted in, (1941-2) 301
- preparation of serum from, (1941-2) 169
- reactions, (1940) 41, (1941-2) 169
- sulphanilamide as preservative, (1941-2) 169
- survival after transfusion, (1941-2) 170
- therapeutic effects, (1940) 42
- use of, (1940) 11
- S. pallida*, survival in frozen plasma, (1944) 102
- substitutes,
 - haemoglobin solution, (1940) 218
 - human serum, (1940) 218
 - sulphanilamide, use of, (1940) 219
- syphilis, transmission by, (1940) 218
- technical improvements in, (1941-2) 42
- technique, (1941-2) 168 (1943) 31, 154
- drip-flow meter, (1940) 221
- gelatin solutions, (1944) 162
- volume and rate, (1940) 222
- toxic effects, (1940) 219
- uraemia after, (1943) 372
- vitamin K in haemorrhagic disease of new-born, and, (1943) 230
- volume and rate, (1940) 222
- volume of blood required, (1940) 36
- war-time, in, (1940) 11
- whole blood, (1940) 11, 222
- gastro-intestinal haemorrhage in, (1941-2) 169
- plasma as substitute for, (1941-2) 169
- Blood vessels,
 - injuries to, (1944) 17
 - soluble rod method of anastomosis, (1941-2) 264
- Blood viscosity in thrombo-angiitis obliterans, (1939) 224
- Blood volume,
 - restoration in shock, (1941-2) 1
 - soluble protein and, (1941-2) 168
- 'Blue drum', (1943) 198
- Body armour, in war, (1940) 11
- Body build in relation to blood pressure, (1941-2) 166
- Body schemes, disturbances of, (1943) 75, 241
- Boeck's sarcoid, (1941-2) 394, (1943) 347
- lacrimal glands, of, (1941-2) 281
- larynx, of, (1941-2) 281
- Boeck's sarcoidosis, (1939) 541, (1940) 533
- Boerner-Lukens modification of Wassermann reaction, (1940) 547
- Boils,
 - treatment,
 - suction, (1941-2) 171
 - sulphathiazole, (1940) 223, (1941-2) 171
- Bombing. *See also* Blast, Crush syndrome
- effect on labour, (1941-2) 19
- Bone,
 - abnormalities, with partial anonychia, (1941-2) 230
 - anaemia, haemolytic, in, (1940) 171
 - carcinoma disease lesions in, (1940) 239
 - carcinomatosis, (1940) 227
 - chondroma, multiple, (1944) 162
 - congenital dystrophies, (1944) 162
 - diseases. *See* Bone diseases
 - dystosis multiplex, (1940) 224
 - dystrophies, (1943) 159
 - congenital, (1940) 224, (1941-2) 171

CUMULATIVE INDEX

Bone—continued

- epiloia, in, (1940) 295
- fenestrate parietales symmetricae, (1940) 224
- fragility, (1941-2) 171
- giant-celled tumour, (1941-2) 172
- grafting, (1940) 277
- haemolytic anaemia, in, (1940) 171
- Hodgkin's disease, (1944) 252
- hydatid cyst of, (1941-2) 259
- lead poisoning, in, (1940) 377
- leontiasis ossea, (1940) 225
- leukaemia in children, changes in, (1940) 384
- Looser's zones, (1941-2) 171
- lymphopathia venereum, changes in, (1940) 398
- lymphosarcoma, (1944) 252
- mandible, congenital hypoplasia, (1940) 224
- melorheostosis, (1944) 163
- myeloid sarcoma, (1941-2) 172
- myeloma,
 - multiple, (1941-2) 173, (1944) 163
 - solitary, (1941-2) 173
- necrosis, aseptic, in carson disease, (1940) 239
- osteoclastoma, (1941-2) 172
- osteogenic sarcoma, (1940) 227
- osteomyelitis, acute, (1941-2) 172
- osteoporosis, (1940) 225
 - post-traumatic, treatment of, (1941-2) 173
- Paget's disease of, (1941-2) 172
- parathyroid hormone, action of, (1944) 316
- polyostotic fibrosis dysplasia, (1944) 162
- pseudo-fractures, (1941-2) 171
- regeneration, (1940) 296
- scurvy, in, (1940) 517
- 'secondary marble', (1940) 172
- tuberculosis, (1943) 160
 - insulin treatment, (1940) 226
- tumours, (1943) 160, (1944) 163
 - benign giant-celled, irradiation treatment, (1943) 160
 - chondroblastoma, benign, (1944) 163
 - ewing's, (1943) 161
 - malignant, (1940) 227 (1941-2) 173, (1944) 163
 - classification and treatment, (1943) 161
 - melorheostosis, (1944) 163
 - multiple myeloma, (1940) 227
 - myeloid sarcoma, (1941-2) 172
 - myeloma, multiple, (1941-2) 173 (1944) 163
 - myeloma, solitary (1941-2) 173
 - non-malignant, (1944) 163
 - phosphatase production in, (1941-2) 172
 - osteoclastoma, (1941-2) 172
 - osteogenic sarcoma, (1943) 161
 - xanthomatosis, (1940) 228
- Bone and joint surgery, (1941-2) 14
- Bone diseases, (1939) 253, (1940) 7, 224 8, (1941-2) 171, (1943) 159, (1944) 162
 - acute osteomyelitis, (1939) 253
 - arachnoidactyly, (1939) 253
 - multiple myeloma, (1939) 254
 - osteitis,
 - condensens, (1939) 253
 - deformans, (1939) 253
- Bone marrow,
 - blood transfusion via, (1943) 155
 - examination of, (1941-2) 6
 - intrasternal introduction of, in aplastic anaemia, (1941-2) 141
 - marble, (1941-2) 171
 - methods of investigating function, (1940) 6
 - spotted, (1941-2) 171
- Boophilus decoloratus*, vector of tick-bite fever, (1940) 81
- Boric acid
 - antiseptic, as, (1944) 13
 - potassium permanganate, powdered, and, (1944) 14
- Bornholm disease, (1943) 162, 282
- Botulism, antitoxin treatment of, (1941-2) 173
- Bournville's disease, (1943) 204
- Brachial artery
 - estimation of blood pressure by palpation of, (1940) 216
 - occlusion of, causing Volkmann's ischaemic contracture, (1940) 195
- Brachial plexus, origin of pain in, (1941-2) 189

Bradycardia

- appendicitis, acute, in, (1943) 130
- diagnosis, (1940) 191
- sign of the unbalanced pendulum, (1940) 191
- treatment of, (1939) 223
- Brain
 - abscess, (1939) 254, (1943) 162 *See also* Abscess, cerebral
 - fungus infection and, (1941-2) 173
 - in relation to congenital heart disease, (1941-2) 174
 - M & B 693 in prophylaxis, (1939) 129
 - middle ear disease complicated by, (1939) 87
 - sulphanilamide therapy, (1939) 255
 - tonsillitis, sequel of, (1939) 254
 - amines, toxic, effects of, (1940) 54
 - anoxia, and mental disease, (1940) 55
 - cerebellar lesions, arm swinging affected by, (1939) 255
 - changes in chronic alcoholism, (1941-2) 134
 - effect on, (1939) 196
 - cysticercosis, radiological diagnosis of, (1941-2) 200
 - diseases,
 - diagnosis by olfactory tests, (1944) 165
 - electric shock, effect of, (1944) 74
 - frontal lobe lesions, (1939) 255, (1940) 71, 228
 - mental changes resulting from, (1940) 71-3
 - function, following cerebral injury, (1941-2) 85
 - fungus infection of, (1941-2) 173
 - glycogen concentration, (1940) 119
 - hyperpathia, determination of areas of, (1939) 256
 - infant, of, (1944) 87
 - injury,
 - intelligence tests in cases of, (1940) 60
 - psychiatric examination in, (1940) 60
 - lesions,
 - hypoglycaemia fatal, in, (1944) 255
 - whooping-cough, in, (1944) 407
 - lobectomy, (1940) 228
 - localization of function, (1941-2) 88
 - metabolism, (1940) 119 (1943) 64
 - oedema, acute, (1944) 184
 - oxidation in, (1940) 119
 - oxygen supply, (1940) 55
 - regional diagnosis, (1939) 255
 - senile plaques, (1943) 113
 - sensory cortex vibratory sensibility, (1939) 256
 - supratentorial lesions, diagnosis by olfactory tests, (1944) 165
 - temperature of different portions of, (1943) 64
 - temporal lobe, lesions of, (1940) 229
 - directional preponderance of nystagmus in, (1944) 88
 - temporo-parietal region lesions, (1939) 256
 - tumour, (1939) 257 *See also* Cerebral tumour
 - bladder mucosa, bony gaps in cranium filled with, (1939) 260
 - cerebral, (1939) 259
 - corpus callosum, of, (1939) 258
 - diagnosis, lipiodol in, (1939) 260
 - differential diagnosis,
 - from general paralysis, (1939) 260
 - from tabes dorsalis, (1939) 260
 - electro-encephalography in, (1939) 124
 - fourth ventricle, of, (1939) 258
 - glioblastosis, diffuse, (1939) 257
 - meningioma, (1939) 257
 - metastatic, (1939) 259
 - prognosis, (1939) 260
 - thalamus, of, (1939) 257
 - third ventricle, of, (1939) 258
 - vascular disorders, (1941-2) 175, (1944) 166
 - whooping-cough causing lesions in, (1943) 379
- Bran, unprepared, constipation treated with, (1941-1942) 197
- Bread
 - national, (1944) 22
 - wholemeal, as source of iron, (1943) 213
- Breast
 - abscess, acute puerperal, (1944) 166
 - carcinoma, (1939) 262; (1940) 231, (1944) 167
 - aetiology, (1940) 231
 - classification, (1939) 262; (1943) 163

CUMULATIVE INDEX

Breast—continued

- carcinoma—continued
 - diffuse metastases in skeleton, (1939) 263
 - endocrine dysfunction, (1940) 231
 - metastatic calcification, (1939) 263
 - inoperable cases, (1944) 167
 - intra-mammary squamous-celled, (1940) 232
 - male breast, of, (1943) 164
 - mucinous, pathology of, (1941-2) 176
 - oestrogen, ingestion of, (1940) 232
 - oestrone, action of, (1940) 231
 - Paget's disease of nipple, (1940) 231, (1944) 167
 - prognosis, (1940) 232; (1943) 163
 - testosterone and progesterone, implantation of, (1943) 164
 - treatment of, (1941-2) 176
 - pre-operative irradiation, (1940) 232
 - results of, (1943) 163
 - X-ray therapy, (1939) 263, (1944) 167
 - diseases of, (1939) 260, (1940) 230-3, (1941-2) 175, (1944) 166
 - aberrant breasts, (1939) 219
 - congenital lesions, (1940) 230
 - surgical treatment of, (1939) 260
 - cysts, (1939) 264
 - engorgement,
 - puerperal, treatment of, (1944) 352
 - testosterone propionate therapy, (1940) 497
 - fat necrosis, carcinoma, diagnosis from, (1939) 262
 - filariasis of, (1943) 211
 - Hodgkin's disease, (1944) 252
 - hormones in relation to, (1939) 264
 - hypertrophy of male breast, endocrine treatment of, (1939) 261
 - inflammation, (1940) 231, (1943) 163
 - testosterone inunction in, (1941-2) 175
 - mastitis, chronic, relation to cancer, (1939) 261
 - nipple discharge, (1941-2) 176
 - oestrin, effect on, (1940) 21
 - pain,
 - hormone therapy, (1944) 52
 - radiography, soft-tissue, (1940) 102
 - sarcoma, (1940) 233
 - supernumerary, (1940) 230
 - tumours, (1940) 231-3, (1944) 167
 - benign, (1943) 163
 - cystosarcoma phyllodes, (1943) 163
 - malignant tumours of, (1941-2) 176
 - irradiation in treatment, (1941-2) 176
 - physical sign of, (1941-2) 176
 - X-ray therapy, (1941-2) 176
 - mixed, (1939) 264
 - oestrogens, in, (1940) 21
- Breast feeding, (1941-2) 262, (1944) 260
 - antirachitic value of human milks, (1940) 346
 - constipation and, (1944) 189
 - control of milk outflow, (1944) 262
 - draught-reflex, (1944) 262
 - prenatal diet of mother, relation to, (1944) 261
 - prolactin, effect in nursing women, (1940) 346
 - social conditions, effect of, (1944) 261
 - teeth, effect on, (1940) 257
 - weaning, avoidance of unnecessary, (1944) 260, 261
 - premature, (1944) 261
 - working mothers and, (1944) 262
- Breathing, deep, effects on peripheral vascular system, (1940) 196
- Breech presentation, aetiology, (1940) 373
- Bridge-of-nose eyelid reflex, (1940) 508
- Brilliant green, blepharitis treated with, (1941-2) 227
- Brilliant vital red
 - convulsions in infancy and childhood, in, (1939) 291
- epilepsy, in, (1939) 333, (1940) 291
- British Pharmaceutical Codex (Third and Fourth Supplements), (1943) 93
- British Pharmacopoeia 1932, (1941-2) 112
 - additional monographs, (1941-2) 112
 - Fourth addendum, (1941-2) 112
 - Fifth addendum 1942, (1943) 93
- Bromethol (avertin), (1940) 127

Bromides

- dosage, (1941-2) 333
- eruptions, treatment by adrenal cortex and sodium chloride, (1941-2) 213
- intoxication, (1941-2) 333, (1944) 350
- Bromine, content of blood, reduction by thyroid extract, (1941-2) 337
- 9-bromo-fluorine, dermatitis caused by, (1940) 258
- 'Bromo-Seltzer', acetamidide poisoning from, (1940) 554
- Bromsulphalein Test, serial, (1944) 288
- Bronchi
 - adenoma, (1941-2) 77, (1943) 60, 270, (1944) 67
 - amyl nitrite, effect of, (1940) 448
 - anatomy, (1943) 58, (1944) 66
 - carcinoma, (1941-2) 77; (1943) 60, 270
 - asthma complicated by, (1943) 138
 - cardiac,
 - infiltration, (1944) 293
 - metastases, (1941-2) 294
 - classification, (1943) 60
 - cutaneous metastases, (1940) 394
 - incidence, (1944) 69
 - intracranial metastases, (1940) 230
 - irradiation, for, (1944) 69
 - lead as aetiological factor, (1944) 294
 - pneumectomy for, (1943) 60, (1944) 69, 294
 - primary, (1941-2) 294
 - X-ray therapy, (1941-2) 374
 - deep, harmful effects of, (1941-2) 372
 - chondroma of, (1941-2) 294
 - dilatation and infection, (1944) 67
 - sarcoidosis of, (1941-2) 295
 - stenosis of, as complication of asthma, (1941-2) 157
 - tumours,
 - malignant, (1941-2) 294
 - non-malignant, (1941-2) 294
- Bronchial spasm, treatment by aminophylline, (1941-2) 158
- Bronchial tree
 - anatomy, (1943) 58, (1944) 66
 - development of, (1943) 58
- Bronchiectasis, (1943) 59
 - aetiology, (1939) 265, (1943) 165
 - allergy, relation to, (1939) 265
 - atelectatic, (1944) 67
 - bronchoscopy, in, (1943) 59, 166
 - causes, (1944) 168
 - clinical picture, (1940) 233
 - cystic, X-ray appearances, (1940) 233
 - forces, in, (1944) 68
 - infection and, (1944) 67
 - pathogenesis, (1944) 67
 - clinical features, and, (1943) 165
 - postural drainage in, (1939) 115
 - pulmonary collapse and, (1944) 67
 - radiological observations, (1944) 67
 - reversible, (1943) 166
 - sinus infection associated with, (1941-2) 127; (1943) 165
 - treatment, (1944) 68, 168
 - bronchoscopy, (1943) 166
 - combined method of, (1939) 266
 - lobectomy, (1939) 265
 - one-stage, (1940) 234
 - sulphapyridine, (1940) 234
 - surgical, (1943) 166
 - prognosis after, (1939) 265
 - X-ray therapy, (1939) 265
- Bronchiolitis, acute, (1941-2) 263
- epidemic influenza, in, (1941-2) 263
- Bronchitis
 - acute catarrhal, tonsillectomy and, (1944) 168
 - chronic,
 - ammonium salts as expectorants, (1941-2) 178
 - expectorants, value of, (1940) 453
 - old age, in, (1944) 170
 - treatment, (1944) 170-2
 - prontosil soluble inhalations in, (1939) 266
 - sulphanilamide and amidopyrine in, (1940) 234
 - treatment, (1944) 170-2
- Bronchography,
 - persistence of lipiodol in lungs after, (1943) 322
 - recent work on, (1944) 66

CUMULATIVE INDEX

Broncho-pneumonia, (1941-2) 177; (1943) 166, (1944) 168
 aetiology, (1944) 168
 aspiration pneumonitis and, (1940) 235
 aspiration type, (1941-2) 177
 bacteriology, (1939) 266
 clinical picture and treatment, (1941-2) 177
 complications, (1944) 168
 foetal, (1939) 31
 infants under one year of age, in, (1941-2) 178
 lipid, (1941-2) 177
 oil aspiration, (1941-2) 177
 mortality, (1944) 168
 primary, (1944) 168
 treatment,
 physiological therapy, (1944) 169
 sulphanilamide and amidopyrine, (1940) 234
 sulphapyridine, (1940) 469-73
 sulphathiazole, (1941-2) 177
 sulphonamide compounds, (1941-2) 177
 young adults, in, (1941-2) 177
 Bronchoscopy
 atelectasis, post-operative, in, (1940) 388
 bronchiectasis, in, (1943) 166
 lung abscess, in, (1941-2) 290
 tuberculosis, in, (1943) 62
 Broncho-spirometry, (1943) 58
 Bronchostenosis as complication of asthma, (1941-1942) 157
 Bronzing of skin, aetiology, (1939) 267 *See also* Pigmentation
Brucella abortus, (1941-2) 416
 infection,
 associated with Hodgkin's disease, (1941-2) 257
 causing acute empyema, (1940) 286
 reaction to sulphonamides, (1941-2) 126
 Brucellosis, cows and pigs, in, (1944) 395
 Bubonic plague, sulphonamides in treatment, (1941-1942) 99
 Buccal neuralgia, (1941-2) 314
 Buccal spots in influenza, (1941-2) 263
 Buerger's disease *See* Thrombo-angitis obliterans
 Bulbar poliomyelitis, after tonsillectomy, (1943) 362
 Bullae, diseases accompanied by, (1944) 318
 Bullet
 lodged in heart, (1941-2) 249
 phosphorus poisoning from exploding, (1944) 19
 tissues, in, lead poisoning from, (1941-2) 282
 Bullous reactions in Schick test, (1941-2) 209
 Bundle-branch block, relation to cardiac enlargement, (1941-2) 150
 Bunions, treatment of, (1941-2) 198
 operation, selection of patients, (1941-2) 198
 Burns, (1941-2) 178, (1943) 167, (1944) 172
 adrenal insufficiency in, (1940) 238
 children, in, (1940) 237
 clinical picture, (1940) 236, (1943) 178
 complex systemic disturbances in, (1941-2) 179
 encephalopathy due to, (1941-2) 178
 eye, of, (1943) 79
 first aid for, (1941-2) 114
 first degree, (1941-2) 178
 fourth and fifth degree, (1943) 169
 histopathological changes in liver, (1941-2) 178
 industrial, (1940) 238
 infected, penicillin and propanidine, use of, (1944) 173
 liver changes in, (1941-2) 178
 mustard-gas, (1943) 80, 167
 neurological after-effects, (1941-2) 178
 pathology, (1941-2) 178; (1943) 167
 plasma loss in, (1941-2) 180
 shock in, (1940) 11, 236; (1941-2) 179
 use of adrenal cortical extract, (1941-2) 181
 systemic disturbances in severe, (1940) 238
 treatment of, (1940) 236-8, (1941-2) 11, 113
 179, (1943) 167, 248
 adrenal cortical extract, (1940) 238; (1941-2) 181
 albucid, (1941-2) 182
 aloes ointment, (1940) 237
 Bunyan-Stannard envelope, (1941-2) 113, 180; (1943) 169
 carron oil, (1941-2) 181
 children, in, (1940) 237

Burns—*continued*
 treatment of—*continued*
 closed-plaster, (1943) 169
 coagulants, (1943) 169
 cod-liver oil, (1940) 238, (1941-2) 181
 cordite explosion, in, (1940) 238
 dyes, (1940) 10, 236-9
 three-dye method, (1940) 236
 functional aspect, (1941-2) 180
 general review, (1941-2) 181
 gentian violet, (1941-2) 181
 glycerin-sulphonamide paste, (1941-2) 182
 hospital, (1941-2) 179, (1943) 305
 hydrosulphosol, (1943) 305
 local, (1941-2) 179
 plasma, (1941-2) 180
 plasma and serum transfusions, (1941-2) 181
 plasma protein transfusion, (1941-2) 180
 propamidine, (1944) 322
 review of, (1943) 169
 silver nitrate, (1941-2) 181
 standard treatment in America, (1943) 168
 sulphadiazine spray, (1944) 172
 sulphanilamides, (1943) 305
 sulphonamides, powdered, (1941-2) 180
 tannic acid, (1940) 10, 236-9, (1941-2) 179, 181
 tulle gras, (1943) 169
 vitamin A, (1940) 128
 war, in, (1940) 10, (1941-2) 179
 warm moist air, (1940) 237
 Burns and scalds, (1939) 267
 adrenal cortical hormone and vitamin C in treatment, (1939) 268
 cement burns, treatment of, (1939) 268
 children, treatment in, (1939) 268
 hydrofluoric acid burns, treatment of, (1939) 267
 infra-red irradiation, (1939) 269
 pathology, (1939) 267
 skin grafting, (1939) 269
 tannic acid and ferric chloride in treatment, (1939) 269
 Bursitis
 acute acromial, surgical treatment, (1940) 300
 radio-humeral, sodium morrhuate therapy, (1940) 300
 subacromial, (1941-2) 189
 subdeltoid, (1941-2) 189
 Butolan, (1943) 94
 trichiniasis, in, (1939) 596
 Butyn, allergy to, (1939) 199

C

Cachexia, differential diagnosis of, (1943) 340
 Cadaver blood, transfusion of, (1940) 38
 Cadmin, poisoning by, (1943) 6, 364
 Cadmium sulphide, tuberculosis, pulmonary, treated with, (1944) 292
 Caecostomy, (1940) 251
 Caecum
 carcinoma of, (1944) 32
 diagnosis, (1944) 33
 operative treatment, (1944) 33
 simple ulcers of, (1941-2) 193
 Caesarean section
 classical operation, (1944) 280
 justifiable abortion, in, (1939) 182
 lower segment operation, (1944) 281
 Caisson disease
 bone and joint lesions, (1940) 239
 helium-oxygen therapy, (1941-2) 182
 treatment of, (1939) 270
 Calcareous degeneration of cornea, (1943) 180
 Calcareous papillitis, (1941-2) 312
 Calcarine fissure, tumour of, causing migraine, (1940) 408
 Calciferol, (1940) 130. *See also* Vitamin D
 keratoconus, in, (1939) 294
 rickets treated with, (1940) 513
 vitamin D₃, relation to, (1939) 18
 Calcification
 cerebral, symmetrical, in hypoparathyroidism, (1940) 432
 coeliac axis, of, (1941-2), 153
 generalized, of intervertebral disks, (1943), 137

CUMULATIVE INDEX

Calcification—*continued*

renal, dissecting aneurysm secondary to, (1941-2) 144

supraspinatus tendon, in, (1941 2) 189

Calcium

absorption in body, (1944) 22

autothiomalate, rheumatoid arthritis treated with, (1944) 153

bilirubinate, faeces, in, (1940) 306

carbonate deposits in gall-bladder, (1940) 306

ether convulsions, in, (1940) 111

excretion, calculi, calcium and, (1940) 366

gluconate, (1941-2) 112

acne treated with, (1940) 147

cardiac oedema treated with, (1941 2) 254

intestinal tuberculosis, in, (1940) 355

infarction, (1941-2) 312

metabolism, (1940) 114

thyrotoxicosis, in, (1943) 223

toxic goitre, in, (1941-2) 236

wholemeal bread, in, (1943) 213

myopia treated with vitamin D and, (1944) 306

neonatal serum, in, (1939) 278

plaques in kidney, (1941 2) 312

pregnancy, requirements in, (1944) 22

present-day diets, in, (1941-2) 232

therapy in convulsions in infancy, (1939) 292

vitamin D and, in myopia, (1940) 417, (1944) 306

Calculus

biliary *See* Gall-stones

pancreatic, (1939) 456, (1941-2) 321, (1943) 296

prostatic, (1940) 482

transurethral removal, (1941-2) 361

renal, (1939) 393, (1940) 366-9, (1941 2) 276

actiology, (1940) 366, (1941-2) 276

alkaline therapy causing, (1940) 366, 442

bilateral, operative treatment, (1943) 257

factors in formation, (1941 2) 276

hydrocele remis associated with pyelonephritis and, (1943) 258

lead, containing, (1941-2) 276

obstructive jaundice due to, (1943) 255

operative X-ray control, (1940) 368

prognosis, (1940) 368

recurrence, factors in, (1940) 368

sulphapyridine causing, (1940) 367, (1943) 257, (1944) 278

sulphathiazole causing, (1940), 367, 461

sulphonamide compounds causing, (1940) 367, 457, 461

vitamin deficiency as factor in, (1940) 14, 366

ureteral,

avertin, treatment with, (1941-2) 276

clinical picture, (1941 2) 276

diagnosis, (1940) 368

insulin-free pancreatic extraction, (1940) 368

pneumopyelography, (1940) 368

prostigmin in treatment, (1940) 369

surgical removal, (1941-2) 276

transurethral manipulation, (1940) 368

urinary, (1940) 366-9

actiology, (1940) 366

calcium excretion, (1940) 366

clinical picture, (1940) 367

diet, influence of, (1940) 366

prophylaxis, (1940) 368

recurrence, (1940) 368

sulphonamide treatment causing, (1944) 329

treatment, (1940) 368

vesical,

mortality from operations on, (1939) 243

sulphapyridine therapy causing, (1941-2) 161

Calomel ointment, impetigo contagiosa treated with, (1940) 345

Calories, requirements of normal and premature infants, (1943) 246

Calvé's disease, (1940) 539

Calvities

actiology, (1944) 129

androgens and, (1944) 129

male hormone in relation to, (1944) 129

Campolon in tropical megalocytic anaemia, (1939) 204

Canal of Nuck, hydrocele of, (1941-2) 330

Cancer, (1939) 270, (1941-2) 182; (1943) 171; (1944) 173 *See also* Carcinogenic agent, Carcinoma, Malignancy, Tumours

abortifacient action of serum and urine from patients with, (1940) 241

advances in knowledge of, (1940) 7

actiology, (1940) 239, (1941-2) 183, (1944) 174

pathology, and, (1939) 270

biopsy material, quantitative examination of, (1941-2) 184

carcinogenic,

properties of coal-tar, (1940) 7

substances, (1940) 239 *See also* Carcinogenic agent

children, in, (1944) 173

chronic mastitis, relation to, (1939) 261

curability in early stages, (1940) 7

diagnosis by biochemical methods, (1941-2) 183

diagnosis, dangers of delay, (1944) 175

diet and, (1940) 240

effects of oestrogen and androgen on cancer tissue, (1941-2) 183

experimental, (1940) 7, (1943) 171, (1944) 173

gastric, gastritis, relation to, (1939) 48

nematode causing, in animals, (1940) 240

hereditary liability, (1939) 270

incidence, (1944) 173

lymph nodes, treatment of, (1940) 14

malignancy, gradation of, (1943) 370

methylcholanthrene causing, (1940) 239

mice, in, (1940) 7

mule-spinner's, (1941-2) 392

pain,

low-temperature treatment in, (1941-2) 184

relief from use of cobra venom, (1941 2) 184

subarachnoid injections of alcohol for, (1941-2) 185

pathology, (1940) 239 41, (1941 2) 183

periodicity hypothesis, (1939) 271

pharynx and larynx, of, treatment of, (1939) 90

primitive races not exempt from, (1940) 7

prognosis, (1940) 241

research, progress of, (1940) 7

review of present-day situation, (1944) 175

sedimentation of red cells in, (1941 2) 163

sex hormones in relation to, (1940) 7

soldiers, in, (1943) 12

treatment, (1940) 242, (1941 2) 13

antipyretic drugs, (1941-2) 339

cobra venom, (1941 2) 184

gonad extracts, (1941 2) 184

fever therapy and irradiation, (1944) 175

low-temperature, (1941-2) 184

radioactive phosphorus, (1943) 171

radiotherapy, (1939) 28, (1940) 242, (1941-2) 184

post-operative, (1944) 175

quantitative examination of biopsy material, (1941-2) 184

super-voltage therapy, (1939) 271

surrounding tissue, in, (1941-2) 185

radium therapy, (1939) 272

refrigeration, (1941-2) 350

surgery and irradiation of, (1939) 28

surgical, (1940) 14, (1943) 13

uniovular and binovular twins, in, (1941-2) 254

Cancer oris, gangrene antitoxin in, (1940) 242

Canine distemper, (1940) 4

Capillary

fragility and permeability, effect of vitamin P on, (1941-2) 426

fragility, vitamins in relation to, (1940) 130

haemorrhage, vitamins in relation to, (1940) 130

intercapillary glomerulo-sclerosis and diabetes mellitus, (1941-2) 152

Carbarsone, amoebic dysentery, in, (1940) 136

Carbohydrate

dietary, high, in pulmonary tuberculosis, (1941-2) 293

tolerance, in hypothyroidism and hyperthyroidism, (1941 2) 306

Carbohydrate metabolism

adrenal cortex and, (1943) 280

brain, in mental diseases, of, (1943) 64

CUMULATIVE INDEX

Carbohydrate metabolism—*continued*

- fat, and, (1943) 32
- infection, and, (1941-2) 306
- lipotropic factors, (1943) 35
- Carbon dioxide
 - absorber, for ether anaesthesia, (1944) 136
 - cyclopropane anaesthesia, CO₂ absorption technique in, (1940) 109
 - solid, endocervicitis treated with, (1940) 289
- Carbon disulphide poisoning, fumes, (1941-2) 411
- mental symptoms following, (1943) 365
- viscose rayon workers, in, (1943) 365
- Carbon monoxide poisoning, (1940) 554
- hypertension caused by, (1940) 212
- mental and neurological sequelae, (1941-2) 408
- Carbon tetrachloride poisoning, (1941-2) 411
- Carbuncle, (1939) 516
- renal, (1943) 259
- treatment,
 - radiotherapy, (1939) 516
 - suction, (1941-2) 171
 - sulphathiazole, (1941-2) 171
- Carcinogenic agents, (1944) 174
- anthracene, (1943) 171
- chemical irritants, (1944) 174
- chrysene, (1943) 171
- oestradiol benzoate, (1941-2) 183
- oestrogens, (1940) 231, (1941-2) 183
- progesterone as anti-tumourigenic agent, (1940) 527
- sex hormones, (1944) 173
- stilboestrol, (1940) 521, (1941-2) 183
- Carcinogenic effect of ultra-violet rays, (1941-2) 129
- Carcinoid tumour
 - appendix, of, (1944) 148
 - colon, of, (1943) 177
 - ileum, of, (1943) 253
 - rectum, of, (1944) 359
- Carcinoma. *See also* Cancer
 - acanthosis nigricans associated with, (1943) 103
 - adrenal cortex, of, (1943) 107
 - anus, of, (1941-2) 147
 - bladder, of, (1943) 144
 - breast, of, (1939) 262, (1943) 164
 - metastasis from, cause of diabetes insipidus, (1939) 301
 - mucinous, (1941-2) 176
 - bronchi, of, (1941-2) 77, 294, (1943) 60, 138, (1944) 69
 - treatment by pneumonectomy, (1943) 60, 272
 - biomimetic, atypical, (1943) 270
 - caecum, of, (1944) 32
 - cervix uteri, (1939) 588
 - radium therapy in, (1943) 20
 - check, of, (1941-2) 308
 - radium therapy, (1940) 504
 - tobacco chewing and, (1941-2) 308
 - colon, of, (1941-2) 194, (1943) 177
 - ascending, (1944) 32
 - corpus uteri, of, (1943) 373
 - duodenum, of, (1943) 254
 - Fallopian tubes, of, (1941-2) 320
 - fat necrosis of breast, differential diagnosis, (1939) 262
 - gastroscope in diagnosis of early, (1939) 21
 - genital, subarachnoid injections of alcohol in, (1941-2) 185
 - inclusion bodies in multiple, (1944) 123
 - jejunum, of, (1943) 254
 - primary, (1941-2) 272
 - large intestine, of, in twins, (1939) 288
 - larynx, of, (1943) 262
 - limbus, of, (1940) 252
 - lips, of, (1943) 281
 - liver, of, (1941-2) 289
 - lung, of, (1939) 115, 415, (1941-2) 294, (1943) 60, 270
 - Meckel's diverticulum, of, (1943) 102
 - melanotic,
 - coloured races, in, (1940) 534
 - radio-sensitivity, (1939) 541
 - mouth, of, (1939) 435, (1941-2) 308
 - nails, of, (1939) 441
 - neck, of, (1939) 442
 - oesophagus, of, (1943) 293

E.M.S. II

Carcinoma—*continued*

- ovary, of, (1941-2) 319
- pancreas, of, (1943) 296
- head of, (1941-2) 321
- penis, of, (1939) 465, (1941-2) 325
- pharynx, of, (1943) 309
- Plummer-Vinson syndrome, associated with, (1939) 185
- post-cricoid, (1943) 309
- prostate, of, (1941-2) 361
- radiotherapy in, (1939) 517, 540
- rectum, of, (1939) 519, (1941-2) 375
- sebaceous glands, of, (1943) 345
- skin, of, (1943) 346
- squamous-celled,
 - anus, of, (1941-2) 147
 - intra-mammary, (1940) 232
- stomach, of, (1941-2) 400
- achalasia of the cardia, supervening on, (1941-2) 128
- thyroid, of, (1940) 241
- tonsil, of, (1941-2) 349
- trachea, of, (1939) 573
- ureter, of, (1941-2) 277
- vagina, of, (1939) 601
- vesical, X-ray therapy for, (1939) 242
- Carcinomatosis, bone, of, (1940) 227
- Cardiac
 - arrest, resuscitation in, (1943) 326
 - circulation, roentgen-cinematography of, (1944) 355
 - compression, treatment of, (1940) 337
 - contusion, (1943) 1
 - diopry, mercurial diuretics and urea in, (1940) 337
 - hypertrophy, (1943) 240
 - infarction. *See also* Infarct
 - atypical, in coronary thrombosis, (1944) 141
 - rupture of interventricular septum due to, (1941-2) 146
 - injuries, (1944) 273
 - insufficiency, vitamin B₁ deficiency and, (1940) 586
 - ischaemia, surgical treatment of, (1940) 15
 - murmurs, diminished attention paid to, (1940) 5
 - neurosis, (1943) 231
 - oedema, mercurial diuretics in, (1943) 1
 - output, angiotom effects of, (1943) 150
 - reserve, (1944) 250
 - factors reducing, (1943) 240
 - sphincter,
 - achalasia, (1941-2) 128, (1943) 104
 - oesophageal ulcer associated with, (1940) 145
 - symptomatology in 'mega' syndromes, (1944) 85
 - tonics, (1944) 321
- Cardiazol. *See also* Leptazol
 - barbiturate poisoning treated with, (1940) 558
 - blood pressure during fit, (1940) 492
 - bradycardia, in, (1939) 223
 - contra-indicated in heart failure, (1939) 60
 - convulsion therapy in schizophrenia, (1939) 499
 - depressive and manic psychoses, in, (1940) 487
 - epilepsy,
 - in diagnosis of, (1939) 332
 - in treatment of, (1939) 333
 - hysterical stupor treated with, (1944) 341
 - (metrazol), (1939) 164 (1941-2) 79
 - schizophrenia, in, (1940) 490 3
 - shock treatment of mental disease with, (1939) 116
- Cardio-omentopexy, (1939) 20, (1940) 183
- Cardiospasm, (1943) 104, (1944) 121
- achalasia and, (1940) 146
- theories of, (1940) 146
- treatment, (1940) 146
- anaesthesia, spinal, (1940) 146
- nitrites, (1940) 146
- Cardiotrophic properties of sex hormones, (1941-2) 381
- Cardiovascular
 - aspects of aviation medicine, (1943) 140
 - diseases, (1939) 56; (1941-2) 1, 44, (1943) 1
 - advances in knowledge of, (1940) 5
 - aetiology of, (1940) 5
 - examination,
 - clinical, (1939) 56
 - special, (1939) 59

CUMULATIVE INDEX

Cardiovascular—continued

- diseases—continued
 - hydrotherapy in, (1939) 377
 - medical treatment, (1939) 59
 - myxoedema, association with, (1943) 286
 - radiology in, (1940) 5
 - recruits, in, (1941) 2) 44
 - surgical treatment, (1939) 60
 - syphilitic, (1940) 5
 - disorders, vitamin B₁ deficiency and, (1941-2) 423
 - stability, and flying, (1941-2) 30
 - system,
 - anthracosis, in, (1940) 188
 - benzedrine, effect of, (1940) 449
- Cardophyllin. *See* Theophylline ethylene diamine
- Caroid, ganglion treated by injection of, (1941-2) 243
- Carotene, (1940) 585
- Carotenoids
 - blood, in, (1940) 116
 - vitamin A and, (1940) 116
- Carotid
 - artery, internal aneurysm of, (1939) 214
 - causing aural haemorrhage, (1941) 2) 144
 - kinked, stimulating aneurysm, (1940) 180
 - body tumours, (1943) 287
 - sinus, (1941) 2) 2
 - reflex, hyperactivity of in coronary disease, (1943) 126
 - stimulation of, causing cerebral thrombosis, (1943) 129
 - syndrome, symptoms and treatment, (1943) 354
- Carotinaemia, (1939) 267
- Carpal cuneiform bone, fractures of, (1943) 194
- Carpal scaphoid, fractured, internal fixation of, (1941-2) 211
- Carriers
 - diphtheria, treatment by sulphathiazole snuff, (1943) 171
 - disinfection of hospital equipment, (1941-2) 185
 - pemphigus neonatorum, (1941) 2) 325
 - typhoid fever, (1944) 223
- Carron oil, burns treated with, (1941) 2) 181
- Carrots, dermatitis caused by, (1941) 2) 203
- Cartilage, radiography, (1940) 102
- Castle's intrinsic factor, (1943) 3, 47
- Castrates, treatment with testosterone propionate, (1939) 534
- Castration, carcinoma of prostate treated by, (1943) 313, (1944) 94
- Cat, neuroses, experimental, in, (1944) 344
- Cataplexy, (1941-2) 311, (1943) 287
- Cataract, (1939) 272
- aetiology, (1940) 243
- allergic eczema and, (1941-2) 137
- associated with tetany and osteomalacia, (1941-2) 186
- diabetic, (1944) 177
- electric current, high-tension, causing, (1940) 243
- para-dichlorobenzene vapour, inhalation of, causing, (1940) 243
- pre-operative injection of typhoid-H antigen, (1940) 243
- surgery, (1939) 272
- treatment, (1940) 243
- vitamin C deficiency associated with, (1939) 272
- Cataracta tetanica, (1941-2) 186
- Catarrh, nasopharyngeal, vitamin A therapy in, (1940) 128
- Catarrhal jaundice. *See* Jaundice, catarrhal
- Catatonica, periodic, nitrogen balance in, (1941-2) 84
- treatment, (1940) 487
- Catatonic pupil, (1944) 348
- Catgut, (1944) 15, 18
- Catholysis, angiomas of retinae treated by surface diathermy and, (1941-2) 377
- Cat itch, (1941-2) 390
- Caudal anaesthesia, in labour, (1943) 18, (1944) 281
- Cauterization
 - chronic cervicitis treated by, (1941-2) 221
 - gas gangrene, in, (1940) 310
- Cavernous sinus
 - thrombophlebitis, heparin and sulphonamide therapy, (1941-2) 408

Cavernous sinus—continued

- thrombosis, (1943) 14
- penicillin in treatment, (1944) 13
- Cavities, tuberculous, (1941-2) 77
- Cavum vergae, cyst of, (1941-2) 175
- Cellophane dressing for wounds, (1940) 349
- Cement burns, treatment of, (1939) 268
- Centenarians, (1941) 2) 379
- rarity of, (1940) 518
- Central Medical War Committee, (1944) 3
- Central nervous system
 - lead poisoning, in, (1943) 263
 - lesions, whooping-cough, in, (1944) 407
 - rehabilitation after injuries to, (1943) 315
 - respiration of, (1940) 119
 - thrombosis, venous, (1940) 66
 - torulosis of, (1944) 383
 - vitamin E in relation to, (1940) 69
- Cephalic tetanus, (1943) 361
- Cephalin-cholesterol flocculation test, (1944) 288
- Cerebellar
 - abscess, otogenic, (1943) 162
 - angioma, funicular, (1943) 127
 - cortex, atrophy of, (1944) 177
 - diseases, (1939) 273
 - Guillain-Barre's syndrome, cerebellar form of, (1939) 273
 - spino-ponto-cerebellar atrophy, (1939) 273
- Cerebral
 - abscess,
 - lingual infection and, (1941) 2) 173
 - relation to congenital heart disease, (1941) 2) 174
 - aneurysm. *See* Aneurysm, cerebral
 - angiography, (1940) 103
 - anoxia, (1944) 159
 - arteriography, (1940) 103
 - arteriosclerosis, (1943) 134
 - artery, anterior, thrombosis of, after stimulation of carotid sinus, (1943) 129
 - atheroma, (1944) 166
 - calcification, symmetrical, in hypoparathyroidism, (1940) 432
 - circulation,
 - mental disease, in, (1940) 56
 - sex-hormones, effect of, (1940) 56
 - concussion. *See* Concussion
 - cortex,
 - basal ganglia, and, survey of physiology of, (1939) 121
 - development of, (1944) 87
 - human electro-corticograms, (1943) 77
 - thalamic influences, (1940) 64
 - thalamus and cortical activity, (1941-2) 89
 - cysticercosis, radiological diagnosis of, (1941-2) 200
 - diplegia, (1939) 273
 - aetiology, (1939) 274
 - clinical picture, (1939) 274
 - embolism. *See* Embolism, cerebral
 - fat embolism, triazol convulsant therapy causing, (1941) 2) 368
 - hemispheres, (1941-2) 88
 - oedema,
 - acute, (1944) 184
 - demyelination caused by, (1939) 124
 - associated with tumours, (1939) 125
 - stromal tumours of choroid plexus, (1941-2) 175
 - symptoms,
 - in trichiniasis, (1943) 366
 - sodium sulphapyridine therapy causing, (1941-2) 187
 - thrombophlebitis, in puerperium, (1943) 318
 - tumours, (1941-2) 174, (1944) 165
 - acoustic neurofibroma, (1941-2) 174
 - angiography, cerebral, (1940) 103
 - arteriography, cerebral, (1940) 103
 - cavum vergae, cyst of, (1941-2) 175
 - choroid plexus, stromal tumours of, (1941-2) 175
 - corpus callosum, (1940) 230
 - diagnosis by ventriculography and encephalography, (1941-2) 175
 - differential diagnosis, (1944) 165

CUMULATIVE INDEX

Cerebral tumours—continued

- encephalography, (1944) 165
- ventriculography in diagnosis of, and, (1941–1942) 175
- erythraemia complicated by, (1944) 231
- headache, localized, in, (1944) 165
- lead encephalopathy simulating, (1941–2) 282
- medulla, of, (1940) 229
- metastatic, (1940) 230
- mid-brain, of, (1940) 229
- migraine caused by, (1940) 408
- neurofibroma, acoustic, (1941–2) 174
- pons, of, (1940) 229
- tuberculomas, (1940) 230
- ventriculography, (1944) 165
- veins,
 - puerperal thrombosis, in, (1943) 4
 - thrombosis of, (1941–2) 92
 - childbirth, after, (1941–2) 407
- ventriculography and encephalography in diagnosis of, (1941–2) 175
- Cerebro-retinal syndromes, (1943) 172
- Cerebrospinal fever, (1939) 274, (1941–2) 184, (1944) 177
- B. enteritidis* infection complicating, (1941–2) 186
- chronic form, (1940) 244
- clinical picture, (1940) 244, (1941–2) 186
- complications and sequelae, (1941–2) 186
- diagnosis, (1941–2) 65, 186
- double infection, (1941–2) 186
- meningeal washing, (1939) 276
- meningococcal,
 - infection without meningitis, (1943) 5, 172
 - septicaemia (1941–2) 186
- mortality, (1944) 177–9
- opsonic index in, (1941–2) 186
- prognosis, results of chemotherapy, (1944) 177
- prophylaxis, (1941–2) 65, 187
- treatment, (1941–2) 65, 187
 - M & B 693, (1939) 274, 276 (1940) 134
 - present war, during, (1944) 11
 - protosol, (1940) 244
 - serum, (1939) 274
 - chemotherapy, and, (1943) 172
 - sulphonamide drugs, and, (1939) 275
 - sodium sulphapyridine, (1941–2) 187
 - sulphanilamide compounds, (1940) 134, 244
 - serum, and, (1940) 245
 - sulphapyridine, (1941–2) 187, (1944) 177
 - serum, and, (1941–2) 187
 - sulphathiazole, (1941–2) 187
 - sulphonamide drugs (1941–2) 65, (1944) 178
 - L.O.S., (1943) 307
 - uleron, (1939) 275
- Waterhouse-Friderichsen syndrome associated with, (1941–2) 186
- Cerebrospinal fluid, (1939) 276, (1943) 172
- alkalosis, in, (1940) 159
- hydrochloric acid and colligol test, (1941–2) 188
- lumbar puncture, indications and contra-indications, (1939) 276
- meningitis, chloride content in, (1940) 406
- osmotherapy, (1939) 277
- pathology, (1941–2) 188
- Prausnitz-Kustner reaction, (1940) 278
- pressure,
 - continuous recording of, (1941–2) 188
 - histamine phosphate injections, effect of, (1941–1942) 188
- proteins, leptazol and insulin-shock therapy, effect of, (1941–2) 368
- sources of contamination in lumbar puncture, (1943) 173
- typhus, in, (1940) 571
- Cerebrospinal rhinorrhoea, bifrontal craniotomy, (1941–2) 188
- Cervical
 - aerocele, (1941–2) 311
 - glands, enlarged in lymphopathia venereum, (1940) 398
 - pre-ganglionectomy for ischaemia, (1939) 61
 - pregnancy, (1940) 481
 - rib, (1941–2) 189, (1943) 173
 - incidence of, (1939) 277
 - scalenus muscle syndrome, (1940) 245

- Cervical-brachial syndrome, (1943) 173
- Cervicitis, (1939) 330
- bismuth therapy causing, (1940) 550
- carbon dioxide, solid, in, (1940) 289
- chronic,
 - survey of, (1939) 33
 - treatment of, (1941–2) 221
- coagulation and ionization, (1940) 288
- hormonal influences, (1940) 22
- infective arthritis, source of, (1939) 228
- irritable bladder due to, (1941–2) 21
- treatment, (1939) 34
- novocain injection, (1940) 289
- pathology of, (1940) 22
- treatment of, (1939) 330, (1940) 288
- Cervico-thoracic sympathectomy, acrocyanosis treated by, (1941–2) 226
- Cervix uteri
 - abdominal pain originating in, treatment of, (1939) 34
 - adenoma, hyaline, (1940) 577
 - carcinoma, (1940) 578
 - endometriosis associated with, (1941–2) 419
 - occurring before age of twenty, (1940) 578
 - radium, interstitial, (1940) 578
 - treatment,
 - local refrigeration, (1941–2) 419
 - radium and X-rays (1941–2) 373, 419, (1943) 20
 - urinary tract, effect on, (1940) 578
 - erosion, (1940) 22
 - failure of dilatation of os, (1941–2) 279
 - granuloma, ulcerative, of, (1940) 322
 - hydrogen ion concentration, (1940) 22
 - labour, role in, (1940) 372
 - obstructions in, (1941–2) 279
 - pregnancy in, (1940) 481
- Cetyl alcohol (1943) 96
- Cetyl trimethyl ammonium bromide (CTAB),
 - surgery, uses in, (1944) 321
- Chamomile flowers, (1939) 472
- Chancroid, (1939) 277, (1941–2) 109
- circumcision for (1939) 278
- diagnosis, (1940) 91
- prevention and treatment, (1944) 106
 - sulphonamides in, (1944) 106
- treatment, (1940) 91
 - dmekos, (1940) 91
 - sulphanilamide, (1940) 245, (1941–2) 189
 - sulphonamide, (1940) 91
 - uleron and protosol in, (1939) 277
- Chaoul technique of radiotherapy, (1940) 105
- Cheilitis
 - lip-stick causing, (1941–2) 203
 - pellagra, in, (1940) 435
- Chemical workers, porphyrinuria in, (1940) 562
- Chemicals, carcinogenic action of, (1944) 174
- Chemotherapy, (1943) 5, 54, 62, 72, 81, 85, 98, 304
- See also* Sulphonamides
- acute osteomyelitis, in, (1941–2) 172
- advances in, (1940) 3
- cerebrospinal fever, in, (1944) 177–9
- endocarditis, subacute bacterial, in, (1943) 237
- fractures, compound, in, (1944) 206
- general paralysis of insane, in, (1941–2) 315
- gonorrhoea, in, (1941–2) 237, (1944) 243
- hypertension associated with renal disease, (1941–1942) 165
- infections,
 - complicating diabetes mellitus, (1943) 187
 - intrapentoneal, (1941–2) 13
- infectious diseases, in, (1943) 54, 306
- iontophoresis in ophthalmology, by, (1944) 220
- laryngo-tracheobronchitis, in, (1941–2) 281
- lupus erythematosus, in, (1943) 273
- meningitis, pneumococcal, in, (1943) 280
- ophthalmology, in, (1943) 81
- otolaryngology, in, (1941–2) 216
- otology and laryngology, in, (1941–2) 56
- penicillin in, (1941–2) 338
- peritonitis, in, (1944) 14
- pneumonia, in, (1943) 306, 310
- protozoal infections, in, (1940) 78
- puerperal sepsis, in, (1944) 353
- pulmonary tuberculosis, in, (1943) 62

CUMULATIVE INDEX

Chemotherapy—*continued*

- recent developments in, (1944) 111-17
- rheumatism, juvenile, in, (1944) 362
- serum therapy in pneumonia, and, (1941-2) 354
- serum therapy versus, (1940) 3
- surgery, application to, (1940) 12
- synthetic, (1940) 3
- tropical diseases, in, (1941-2) 99
- urinary infections, in, (1943) 72, 304
- virus disease, in, (1944) 321
- war wounds, in, (1941-2) 10
- wound infection, in, (1941-2) 265
- wounds, in, (1940) 10, (1943) 9, 305
- Chest**
 - emphysematous form of, (1941-2) 219
 - injuries, (1941-2) 71, 75
 - blast, (1941-2) 3
 - stresses, and, non-penetrating, (1944) 273
 - mass radiography of, (1940) 103, 503
 - significance of small intracutaneous vein on, (1941-2) 421
 - wounds, (1941-2) 71, 75, (1943) 9, 247
 - artificial pneumothorax in treatment of, (1940) 349
 - drainage of pleura in, (1943) 249
 - non-penetrating, coronary thrombosis due to, (1944) 140
 - treatment, (1943) 9, 305, 311
 - X-ray examination in erythraemia, (1943) 206
- Cheyletiella parasitivorax*, (1941-2) 390
- Chicken-pox**
 - acute pemphigus complicating, (1941-2) 189
 - encephalitis complicating, (1943) 173
 - herpes zoster and, (1940) 246, (1941-2) 255
 - neurological complications, (1941-2) 189
 - pneumonia complicating, (1943) 173
- Chilblains**, (1943) 1, 173
 - treatment, (1944) 179
 - Bier's method, (1944) 179
- Child**
 - adiposity in, (1941-2) 130
 - allergy, gastro-intestinal, in, (1940) 163
 - anaemia, nutritional, in, (1944) 131
 - anaesthesia in, (1940) 111
 - antenatal care, advances in, (1939) 37
 - appendicitis in, (1943) 130
 - acute, (1944) 147
 - banana in diet, (1941-2) 262
 - burns in, (1940) 237
 - cancer in, incidence, (1944) 173
 - cirrhosis of liver in, (1940) 387
 - coarctation of aorta of adult type in, (1944) 151
 - diseases of, (1939) 37, (1941-2) 48
 - eosinophil leukaemia in, (1943) 265
 - fate of, after threatened abortion, (1943) 16
 - feeding of, (1941-2) 262
 - flat-foot, congenital, in, (1944) 236
 - gastro-intestinal allergy in, (1940) 163
 - glomerulo-nephritis, acute, in, (1941-2) 313
 - growth and development, (1944) 180
 - Gurllain-Barre syndrome in, (1941-2) 315
 - health and welfare of, (1939) 278
 - neonatal diarrhoea, prevention of, (1939) 278
 - neonatal serum calcium, (1939) 278
 - heart disease, rheumatic, in, (1944) 248
 - hyperparathyroidism in, (1940) 433
 - hypertension, essential, in, (1941-2) 164
 - malignant, (1941-2) 164
 - idiopathic cardiac enlargement in, (1943) 233
 - infant mortality, reduction of, (1939) 37
 - kala-azar in, (1940) 363
 - laryngeal cancer in, (1943) 263
 - lead encephalopathy in, (1941-2) 282
 - lead poisoning in, (1940) 377
 - leukaemia, bone changes in, (1940) 384
 - malaria in, (1940) 399
 - mastoiditis in, (1943) 198
 - myasthenia gravis in, (1943) 283
 - nephritis in,
 - acute, (1940) 420
 - tonsillectomy, effect of, (1940) 422
 - nephrotic crisis in, (1940) 421
 - nutrition of, (1941-2) 49
 - nutritional anaemia in, (1943) 215
 - obese, treatment, (1941-2) 130

Child—*continued*

- ophthalmia, epidemic gonorrhoeal, in, (1943) 178
- osseous tuberculosis in, (1943) 160
- oxuriasis in, (1941-2) 311
- peptic ulcer in, (1941-2) 326, (1943) 300
- pneumonia in, (1941-2) 355
 - portal phlebosclerosis, primary, in, (1943) 351
- psychiatry of, (1941-2) 362, (1943) 314
- rheumatic fever in, (1941-2) 377
- rheumatic heart disease in, (1943) 234
- rheumatism, acute, in, (1944) 360-2
- scabies in, (1944) 372
- tuberculous infection in, (1944) 392
- vitamin requirements of, (1943) 213, 377
- vulvo-vaginitis in, (1940) 319
 - gonococcal, (1943) 91, 226
- Child-birth, presacral neurectomy, after, (1940) 546
- Chiniolin, enema, in amoebic dysentery, (1940) 167
- Chloride, content of cerebrospinal fluid in meningitis, (1940) 406
- Chlorinated hydrocarbons, poisoning by, (1941-2) 411
- Chlorinated naphthalene, acneriform reactions and acute yellow atrophy caused by, (1944) 387
- Chloroform anaesthesia, relative safety, (1940) 109
- Chloroma, (1941-2) 285
 - morbid anatomy, (1944) 285
- Chlorophyll, antiseptic action of, (1941-2) 333
- Chlorosis, (1941-2) 139, (1943) 117
 - minerals in diet, need for, (1944) 132
- Chloroxyleneol, (1943) 94
- Choana, congenital occlusion of, (1939) 183, (1940) 144
- Cholangiography, (1940) 13
- Cholangitis, (1939) 347
 - adrenal hormone therapy, (1939) 347
 - benign stricture of common and hepatic ducts, (1940) 307
 - lenta, (1939) 348
 - micro-organisms found in, (1939) 49
 - prontosil treatment, (1939) 347
 - surgery, (1939) 348
- Cholecystitis, (1939) 346
 - acute, aneurysm of coeliac artery simulating, (1941-2) 143
 - chronic, in old age, (1940) 307
 - cystic duct lesions, (1939) 346
 - electro-surgical obliteration, (1940) 306
 - morbid anatomy, (1939) 346
 - pancreatic reflex, (1939) 346
 - pathogenesis, (1943) 219
 - post-operative,
 - prognosis, (1939) 346
 - treatment, (1939) 347
 - visualization of gall-bladder by gas, (1941-2) 234
- Cholecystocholedochostomy, (1940) 308
- Cholecystography, (1941-2) 234
 - gall-bladder disorders, in diagnosis of, (1939) 48
 - peristalsis of common bile-duct, (1943) 219
 - pitressin, use of, (1940) 503
- Cholecysto-hepatic flexure, adhesions of, (1940) 307
- Cholecystotomy, old age, in, (1940) 307
- Cholera
 - anuria complicating, (1943) 174
 - prevention, (1944) 100
 - renal reactions in, (1943) 174
 - serological identification, (1944) 100
 - treatment, (1944) 100
 - hypertonic saline, (1944) 100
 - intravenous saline and oxygen in anuria, (1943) 174
 - sulphaguamide, (1944) 100
- Cholesteatoma, ear, of, (1943) 199
- Cholesterol
 - blood values, in general pruritus, (1944) 337
 - faeces, in, (1940) 306
 - granulomatosis, acute idiopathic, (1943) 266
 - hypochromic anaemia of pregnancy, in, (1940) 171
 - serum level, effect of X-rays on, (1941-2) 372
 - cholesterolaemia, psoriasis, in, (1944) 338
- Cholesterosis of gall-bladder, (1941-2) 233
- Cholic acid—vitamin K mixture
 - hypoprothrombinaemia, in, (1940) 358
 - post-operative bleeding, in, (1940) 357

CUMULATIVE INDEX

- Choline
derivatives, in asthma, (1941-2) 333
hydrochloride, erythraemia treated with, (1941-2) 225
member of vitamin B₂ complex, as, (1941-2) 423
- Cholinesterase
index, liver disease, in, (1940) 387
serum determinations in biliary disease, (1944) 287
- Chondritis, knee-joint, of, (1940) 361
- Chondrioblastoma, benign, (1944) 163
- Chondrodysplasia, hereditary, differential diagnosis from achondroplasia, (1943) 104
- Chondroma
bronchus, of, (1941-2) 294
larynx, of, (1943) 41
multiple, (1944) 162
- Chordoma, (1943) 174
- Chordotomy, anterior, for gastric crises in tabes, (1940) 426
- Chorea
aetiology of, (1939) 278, (1940) 5
fever therapy and vitamin B in, (1941-2) 189
Huntington's, (1939) 279
differential diagnosis, (1939) 279
pathogenesis of, (1943) 175
rheumatism, relation to, (1939) 136
- Choreo-athetosis, familial paroxysmal, (1941-2) 159
- Choriomelanoma, (1940) 246
- Chorion, (1941-2) 190
extra-genital, in male, (1941-2) 190
Friedman test, quantitative, in, (1940) 246
hydatidiform mole and, (1940) 246
virgin aged 71, in a, (1940) 247
- Chorionic gonadotrophin, (1941-2) 22
- Choroid
melanoma of, (1943) 374
plexus, stromal tumours of, (1941-2) 175
- Choryl, carbachol, official name for, (1940) 127
- Chromium
poisoning, (1940) 559
trioxide, gingivo-stomatitis treated with, (1941-1942) 307
- Chromoblastomycosis, (1941-2) 233
- Chrysene, carcinogenic effects of, (1943) 171
- Chunine, malaria treated with, (1943) 277
- Chyladenectasis, mesenteric, (1943) 266
- Chylothorax, traumatic, (1943) 276
- Chylous effusion, (1943) 276
- Ciba 3714, (1941-2) 117
- Cibazol, (1941-2) 117
- Cigarette smoking. *See* Smoking
- Cignolin, (1943) 94
- Cinchophen in rheumatoid arthritis, (1939) 227
- Cinematography, roentgen. *See* Roentgen-cinematography
- Cineradiography, (1940) 98 101
films, production of, (1940) 98
direct method, (1940) 99
indirect method, (1940) 99
synthetic method, (1940) 98
future of, (1940) 100
size of field, (1940) 99
- Circulation
athletes, in, (1940) 204
benzedrine, effects of inhalation, (1940) 449
fluids, effects of overloading by, (1944) 322
foetal and placental, (1943) 15
intrahepatic, (1941-2) 288
peripheral, (1944) 81
aminophylline, effect of, on, (1941-2) 331
disorders, (1940) 196
pulmonary, eupaverin, effects of, (1940) 451
- Circulatory disorders of extremities, (1941-2) 226
- Circumcision, chancreoid, in treatment of, (1939) 278
- Cirrhosis
Hanot's unilobular, (1941-2) 289
hepatic. *See* Liver, cirrhosis
xanthomatous biliary, (1941-2) 287
- Cirsoid aneurysms, (1943) 123
- Citrus fruits, toxic dermatitis caused by, (1939) 299
- Clay-shoveller's fracture, (1940) 276
- Climacteric, (1940) 248, 522, (1941-2) 190
disorders, (1939) 279
endocrine factors, (1939) 279
follicular hormone in, (1939) 280
- Climacteric—*continued*
disorders—*continued*
oestrogen therapy, (1939) 280
female, in, (1940) 247
diabetes mellitus complicating, (1941-2) 191
hyperthyroidism associated with, (1940) 247; (1941-2) 190
treatment,
endocrine therapy, (1941-2) 191
hormone therapy, (1944) 369
oestradiol dipropionate, (1940) 248
oestradiol implantation, (1941-2) 190
oestrin, psychotherapy, and sedation, (1941-1942) 191
oestrogen replacement by hormones, (1943) 334
oestrogen, implantation of, (1943) 20, (1944) 27
oestrone implantation, (1943) 175
oestrone and progesterone in diabetic cases, (1941-2) 191
sex hormones, (1941-2) 384
stilboestrol, (1940) 248, 522, (1941-2) 191, (1943) 98
testosterone propionate, (1939) 536, (1940) 248
theelin pellets, implantation of, (1940) 248
vaginits, (1941-2) 429
male, in, (1941-2) 191
induced, in treatment of migraine, (1940) 409
testosterone propionate in, (1940) 249
treatment, (1940) 249
- Climate in treatment of disease, (1943) 280
mountain sickness, arsenic as prophylactic, (1939) 280
- Climatic and socio-economic factors in relation to disease, (1939) 2
- Clinical science, (1940) 8
- Clitoris, elephantiasis, (1941-2) 430
- Closed-plaster for wounds, (1940) 350
- Clostridium
tetani, toxoid, (1940) 137
welchii,
infection,
abortion followed by, (1939) 182
during pregnancy, (1940) 481
sulphanilamide in, (1941-2) 341
sulphonamides, action on, (1939) 171, (1940) 133
wounds infected by, (1941-2) 267
- Clothing, dyed, dermatitis caused by, (1940) 258
- Clover, anti-haemorrhagic principle in, (1944) 322
- Clubbed fingers, osteoarthropathy, pulmonary, in, (1944) 276
- Coal miners
collier's stripes in, (1940) 259
dyspnoea in, (1939) 322
- Coal-tar, carcinogenic properties of, (1940) 7
- Coarctation of aorta. *See* Aorta
- Coats's disease, (1940) 510
- Cobra venom
arthralgias treated with, (1940) 300
leprosy treated with, (1939) 402
pain,
cancer, treated with, in, (1941-2) 184
carcinoma of cervix uteri, treated with, in, (1941-2) 419
intractable, treated with, (1940) 429
therapeutic uses of, (1943) 303
- Coccidioid
arthritis, (1943) 146
granuloma, (1943) 145
valley fever and, (1944) 157
- Coccidioides immitis, (1943) 205
arthritis of ankles caused by, (1943) 146
coccidioid granuloma caused by, (1943) 145
- Coccidioidomycosis, (1943) 145, 205
- Coccyx diseases, (1939) 281
piloid cyst, sclerotherapy of, (1939) 281
- Cod-liver oil,
aural surgery, in, (1939) 87
burns, treated with, (1940) 238, (1941-2) 181
colitis, ulcerative, in, (1939) 287
dressing for wounds, as, (1940) 350
tuberculosis, treatment of, in, (1941-2) 415
wounds treated with, (1943) 248

CUMULATIVE INDEX

- Celiac**
artery, aneurysm of, (1941-2) 143
axis, calcification and X-ray appearance, (1941-2) 153
disease, (1939) 282, (1941-2) 26
 blood-sugar curve, cause of low, (1939) 282
 clinical picture, (1939) 282
 diagnosis, (1939) 283, (1941-2) 192
 haemorrhagic diathesis associated with, (1941-2) 192
 high protein banana diet in, (1939) 283
 hypovitaminosis of fat-soluble vitamins in, (1941-2) 192
 identical twins, in, (1941-2) 191
 treatment, synthetic vitamin K, (1941-2) 192
 vitamin A absorption test, (1941-2) 192
 vitamin D in treatment, (1939) 283
 vitamin K deficiency in, (1941-2) 192
Coffee beans, impetigo treated with, (1939) 381
Colchicine, effects after partial hypatectomy, (1941-2) 333
Cold. *See also* Cryotherapy
 adiponectosis ex frigore due to, (1941-2) 226
 agglutination, spontaneous, in Raynaud's phenomenon, (1943) 325
 allergy, (1940) 163
 aviation, protection against, in, (1941-2) 35
 chilblains and, (1943) 174
 frost-bite and trench foot, (1944) 239
 immersion-foot and immersion-hand, (1944) 239-240
 limbs, damage to, by, (1943) 1
 shock, effect on, (1941-2) 387
 tissue damage due to, (1944) 239
Cold-pressor test
 hypertension, in, (1940) 216
 pregnancy, in, (1940) 479
Colds, (1939) 283, (1941-2) 193, (1943) 175, (1944) 180
 aetiology, (1939) 283, (1944) 180
 bacteriology, (1944) 181
 essential unsaturated fatty acids in treatment, (1941-2) 193
 intranasal vaccine spray, (1941-2) 193
 nasal sprays, danger of, (1939) 285
 paranasal sinusitis, importance of, (1944) 180
 prophylaxis, (1941-2) 193, (1944) 182
 ultra violet irradiation, (1939) 284
 vaccines for, (1939) 284 (1941-2) 193
 vitamin A, (1939) 284
 treatment, (1941-2) 193 (1944) 182
 sodium sulphathiazole, (1944) 181
Colectomy, ulcerative colitis treated by, (1944) 183
Colic
 drugs in, (1939) 165
 mucous, psychological factors in, (1940) 6
 renal, sulphonamides causing, (1941-2) 346
 treatment of, demerol in, (1944) 321
Coliform bacillus infections, (1939) 285
 mandelic acid in, (1939) 285
 sulphanilamide in, (1939) 285
 sulphonamides in, (1941-2) 100
Colitis, (1941-2) 193
 chronic ulcerative, (1940) 6
 clinical picture, (1941-2) 193
 ulcerative, (1939) 286, (1940) 219, (1941-2) 193
 aetiology, (1943) 176, (1944) 183
 psychological factors in, (1939) 15 286
 allergic phenomenon, as, (1943) 176
 allergy, role of, (1944) 183
 clinical course, (1943) 176
 clinical picture, (1941-2) 193
 cod-liver oil and drug therapy, (1939) 287
 cod-liver oil enemas, (1939) 287
 ileostomy in, (1944) 20
 infantilism, associated with, (1940) 249
 larocain, (1939) 287
 lymphopathia venereum, relation to, (1941-2) 193
 neoprontosil in, (1939) 286, (1940) 249
 Shigella organisms, in relation to, (1939) 286
 sulphanilamide, (1939) 288
 surgery, (1939) 288
 symptoms, (1944) 183
Colitis *continued*
 ulcerative—*continued*
 treatment, (1940) 249, (1944) 183
 colectomy, (1944) 183
 ileostomy, (1944) 20, 183
 liver therapy, (1939) 286
 psychotherapy, (1939) 288
 sulphonamide compounds, (1941-2) 194
 surgical, (1940) 26-8
 vaccine therapy, (1939) 288
 vitamin B₁₂ and liver therapy, (1939) 287
Collapse, (1941-2) 385, (1943) 337. *See also* Shock
 acute fatal non-traumatic, during exertion, (1940) 205
 neosynephrin in treatment, (1940) 528
 paredrinol in treatment, (1940) 529
Collargol test, (1941-2) 188
Collier's stripes, (1940) 259
Colloidal gold reaction, hepatic disease, in, (1940) 386
Collosol B, vitamin B₁₂ preparation, (1940) 129
Collosol K, (1940) 131. *See also* Vitamin K
Colon
 abnormalities of, (1941-2) 231
 adenocarcinoma of large intestine in twins, (1939) 288
 adenomatous polyp of, (1944) 184
 ascending, carcinoma of, (1944) 32
 diagnosis, (1944) 33
 operative treatment, (1944) 33
 carcinoid tumours of, primary, (1943) 177
 carcinoma, (1939) 288, (1940) 250, (1941-2) 194, (1944) 184
 adenomatous polyp associated with, (1944) 184
 cancerostomy, (1940) 251
 clinical picture, (1941-2) 195
 diagnosis of early lesions, (1943) 177
 incidence, (1941-2) 194
 morbid anatomy, (1940) 250
 multiple primary polyp, (1941-2) 195
 one-stage resection, (1941-2) 195
 polyposis and, (1940) 250
 symptoms, (1941-2) 194
 treatment, (1941-2) 195
 developments in diseases of, (1940) 5
 disorders of, (1939) 22
 diverticulitis, obstructing, (1941-2) 212
 proctoscopy in diagnosis, (1944) 207
 polyp, multiple primary, (1941-2) 195
 polyposis, (1941-2) 375, (1944) 184
 familial, (1944) 184
 psychological factors in diseases of, (1940) 6
 multiplication of, (1941-2) 231
 ulcers, simple, of, (1941-2) 193
 water balance in, (1944) 190
Colostomy, diverticulitis, obstructing, in, (1941-2) 212
 perineal, for carcinoma of rectum, (1940) 507
Coloured faces, melanotic carcinoma in, (1940) 534
Colo-vesical fistula, diverticulitis and, (1941-2) 25
Coma
 diabetic, (1943) 36, 187, 245
 condition of eye in, (1943) 36
 prognosis, (1940) 262
 treatment (1943) 187, (1944) 200
 warning symptoms of, (1941-2) 207
 insulin, (1943) 67, 245
Common carotid artery, kinked, simulating aneurysm, (1940) 180
Compensation, Workmen's, psychiatric aspects of, (1943) 69
Complement fixation test
 malaria, in, (1943) 83
 psittacosis, in, (1940) 485
Compressed-air workers, aero-otitis media in, (1941-2) 182
Compression, cerebral, (1944) 184
 treatment, (1944) 185
Compression injuries, (1941-2) 1, 9
Concrete
 as protective material against high-voltage X-rays, (1940) 502

CUMULATIVE INDEX

- Concussion, (1943) 178, 251; (1944) 184 *See also* Blast.
- acceleration, (1941-2) 93
 - compression, (1941-2) 93
 - experimental, (1941-2) 92, 197; (1944) 156
 - haemorrhagic lesions, (1941-2) 94
 - influence of shape of skull, (1941-2) 94
 - lymphopenia after, (1940) 251
 - mechanism of, (1940) 70
 - paralysis, duration of, (1941-2) 94
 - paralytic phenomena, (1941-2) 94
 - post-concussional syndromes, (1940) 251, (1944) 185
 - pulmonary, and blast, (1941-2) 3
 - scalp wounds complicating, (1941-2) 196
 - theory of, (1940) 70, (1941-2) 195
 - treatment, (1944) 185
 - dehydration, (1944) 185
- Concussion and compression, (1939) 289
- diagnosis and treatment, (1939) 289
- Conditioned reflex, alcoholism treated by establishment of, (1940) 158
- Confusional states, acute, adrenal cortical extract in, (1940) 290
- Congenital
- arteriovenous fistula, (1940) 301
 - atresia of oesophagus, (1940) 427
 - cyst of larynx, (1940) 375
 - cyst of round ligament of liver, (1940) 388
 - flat-foot, (1944) 236
 - gottie, fatal sporadic, (1940) 315
 - pyloric stenosis, (1940) 501
 - surgical treatment of abnormalities, (1940) 14
 - syphilis, (1944) 382
 - trypanosomiasis, (1944) 99
- Conglutination of serum, Caesarean section, (1941-2) 279
- Congo red, toxicity and general effects, (1940) 450
- Conjugal neurosyphilis, (1941-2) 403
- Conjunctiva, (1940) 251
- carcinoma, primary, of limbus, (1940) 252
 - diseases, (1941-2) 196, (1943) 178, (1944) 186
 - gonococcal ophthalmia, sulphanilamide in, (1939) 291
 - hypopyon in mine workers, (1939) 290
 - inclusion, sulphanilamide therapy, (1941-2) 196
 - inflammation
 - bacterial, (1944) 186
 - non-bacterial, (1944) 187
 - injury (1944) 186
 - disease, and, (1939) 289
 - lime burns, ammonium chloride treatment of, (1939) 289
 - melanoma, malignant, of, (1941-2) 196
 - ophthalmia neonatorum, sulphanilamide in, (1939) 291
 - tumours, (1941-2) 196, (1943) 207
- Conjunctivitis, (1941-2) 196
- acute papillary, (1939) 290
 - acute staphylococcal, (1944) 186
 - Beal's type, (1944) 187
 - causes in general practice, (1944) 187
 - chronic, sulphonamide treatment, dangers of, (1944) 186
 - chronic unilateral, due to virus of lymphopathia venereum, (1941-2) 300
 - epidemic kerato-, (1944) 187
 - follicular, (1943) 178
 - acute, (1944) 187
 - gonococcal, (1940) 251, (1943) 178
 - inclusion, (1943) 178
 - inflammation, bacterial and non-bacterial, (1941-2) 196
- Koch-Weeks bacillus causing, (1940) 252
- mucopurulent, (1939) 130
- Oligoseptic treatment, (1940) 445
- Polycytenular conjunctivitis, tuberculosis, relation to, (1939) 289
- Silver ferrihaemoglobin in, (1941-2) 339
- Morax-Axenfeld conjunctivitis, (1941-2) 339
- Staphylococcal, acute, (1944) 186
- Staphylococcal, staphylococcus toxoid in, (1939) 290
- Streptococcal pseudomembranous, (1940) 252
- Sulphanilamide in, (1940) 251
- Constipation, (1941-2) 196, (1944) 189
- aetiology, (1944) 189
 - aperients, abuse of, (1944) 190
 - atonic, vitamin B₁ in, (1940) 129
 - biliary, (1944) 190
 - breast-feeding, and (1944) 189
 - gall-bladder and, (1944) 189
 - hygienic routine, need for, (1944) 190
 - pathogenesis, (1944) 190
 - treatment, (1944) 191
 - hemicellulose hydrogels, (1944) 190
 - phenolphthalein, (1944) 190
 - unprepared brain, (1941-2) 197
 - water and bile, importance of, (1944) 190
 - women, in, decrease in, (1940) 5
- Constitution
- cerebrotonia, (1944) 77
 - clinical types and treatment, (1944) 251
 - Kietschmer's types and menstrual history, (1940) 339
 - personality and, (1944) 77
 - somatotonia, (1944) 77
 - viscerotonia, (1944) 77
- Contact lenses, (1939) 132
- Contraception
- jellies, (1941-2) 197
 - 'safe period', (1941-2) 197
 - spermicidal preparations, (1941-2) 197
- Contrast radiography, diodrast and anaphylaxis, (1943) 321
- Convalescence, old age, in, (1940) 518
- Convalescent
- blood, herpes zoster ophthalmicus treated with, (1941-2) 198
 - serum, in prophylaxis of measles, (1941-2) 302
- Convallaria, heart failure treated with, (1940) 338
- Convallaria majalis, (1940) 338
- Convulsion therapy
- ammonium chloride, by, (1940) 59, (1941-2) 368, (1944) 349 *See also* Leptazol shock therapy
 - anxiety states, in, (1941-2) 80
 - cardiazol, (1940) 58, (1941-2) 366-8
 - complications of, (1940) 58
 - compulsion neurosis, in, (1941-2) 364
 - curative, use of, (1940) 59, (1941) 346
 - death after, (1944) 349
 - depressive states, in, (1943) 317
 - electrical method, (1940) 59, 494, (1941-2) 80, 368, (1943) 4
 - mental disease, in, (1941-2) 218
 - fractures and dislocations caused by, (1940) 59, 491, (1941-2) 80
 - insulin shock, (1941-2) 367
 - involutional-depressive psychoses, in, (1940) 488, (1941-2) 79
 - leptazol, (1940) 58, (1941-2) 366-8
 - mechanism, (1940) 58
 - mental disorders, in, (1941-2) 79, (1943) 66
 - nitrogen, inhalation of, (1940) 59, 496
 - picrotoxin, (1940) 59
 - psychology of, (1940) 490
 - schizophrenia, in, (1940) 58, 490-6, (1941-2) 79, (1943) 317, (1944) 348-50
 - spinal anaesthesia in, (1944) 349
 - sub-convulsant doses in, (1941-2) 365
 - technique, (1940) 58
 - traumatic complications, prevention of, (1943) 317
 - triazol, (1941-2) 368
- Convulsions
- anaesthesia, during, (1940) 111, 174
 - epilepsy, in, (1944) 228
 - ether, (1943) 120
 - infancy and childhood, in, (1939) 291
 - aetiology, (1940) 253
 - brilliant vital red in, (1939) 291
 - calcium therapy, (1939) 292
 - dihydrotachysterol in post-operative tetany, (1939) 291
 - ether anaesthesia, under, (1939) 207
 - sodium diphenyl-hydantoinate in treatment, (1941-2) 197
 - treatment, (1940) 253
 - underlying causes, (1941-2) 197

CUMULATIVE INDEX

- Convulsions—continued**
nephritic, treatment by magnesium sulphate, (1943) 289
otogenic origin, of, (1941-2) 216
Cooley's erythroblastic anaemia, (1940) 172, (1941-2) 140
Copper, effect on demyelination in lambs of, (1939) 123
Copper sulphate, ringworm treated by iontophoresis of, (1943) 217
Coproporphyrin, urine, in, (1944) 245
Coproporphyrinuria, alcoholic cirrhosis of liver and, (1944) 245
- Cor**
bi-atriatum triloculare, (1940-2) 248
pulmonale,
chronic, (1941-2) 291
pulmonary emphysema in relation to, (1943) 240
subacute, (1941-2) 252
- Coramine (anacardone),** (1939) 164, (1941-2) 112
alcoholism treated with, (1939) 195
anaesthetic antidote, as, (1939) 212
contra-indicated in heart failure, (1939) 60
effect on abnormal respiratory rate, (1941-2) 334
heart disease, in, (1941-2) 334
nikethamide, official name for, (1940) 127
- Cordite, explosion burns,** (1940) 238
- Cornea**
arcus senilis, aetiology of, (1939) 293
burns, (1943) 79
calcareous degeneration, (1943) 180
chemical injuries, (1944) 192
diseases, (1940) 253, (1943) 179, (1944) 192
examination by means of fluorescein, (1941-2) 226
fluorescein, in various conditions, use of, (1941-2) 226
gas injuries, (1944) 192
herpes zoster, convalescent blood in treatment, (1941-2) 198
hypopyon, treated by sulphonamides, (1941-2) 198
injuries and diseases, (1939) 292 (1944) 192
broken spectacle glass, from, (1940) 253
keratitis, (1940) 254
acute epidemic superficial punctate, (1939) 292
ramificata superficialis, (1939) 293
keratoconus, vitamin D therapy in, (1939) 293
molluscum contagiosum of eyelid and, (1940) 298
mustard-gas lesions, (1943) 80
necroscleritis nodosa, (1940) 254
opacities, intravenous injections of ascorbic acid in, (1941-2) 198
penetration by naphthalene compounds, rate of, (1944) 323
symptomatic affections, (1940) 254
transplantation, (1940) 254
ulcer,
intravenous injections of ascorbic acid in, (1941-2) 198
lenticular changes following, (1944) 192
methyl salicylate treatment of, (1939) 292
sequelae, (1944) 192
sulphanilamide therapy, (1940) 253
sulphonamides in, (1941-2) 198
- Corneal grafting,** (1939) 131
- Corns, soft, treatment of,** (1941-2) 198
- Corns and bunions, aetiology,** (1939) 294
- Coronary**
arteries, rupture, (1941-2) 144
disease,
blood pressure, effect on subsequent course, (1940) 213
cardio-omentalpexy in, (1940) 183
tobacco smoking and, (1941-2) 152
X-ray diagnosis of, (1941-2) 146
occlusion, (1940) 5, (1941-2) 145, (1943) 123 *See also* Coronary thrombosis
correlation of shock and, (1943) 125
thrombosis, (1939) 217, (1940) 5, (1941-2) 144, (1943) 125
cardiac infarction, atypical, (1944) 141
carotid sinus reflex, hyperactivity of, (1943) 126
clinical picture, (1940) 184 6, (1943) 125, (1944) 141
coronary occlusion and, (1941-2) 145
- Coronary—continued**
thrombosis—continued
course and prognosis, (1940) 186; (1941-2) 145, (1943) 125
diagnosis, (1941-2) 146, (1943) 126
embolus of abdominal aorta, (1943) 125
heparin as possible treatment, (1939) 217
industry, in, (1944) 140
intraventricular conduction, disturbances of, (1939) 217
medico-legal aspects, (1944) 141
mortality, immediate, (1941-2) 145
myocardial infarction, (1940) 185
pain, (1941-2) 145
pathology, in relation to clinical picture, (1940) 184 6
premonitory symptoms, (1941-2) 145
prodromal pain, (1941-2) 145
radiographical criteria for diagnosis, (1939) 217
rehabilitation, (1941-2) 146
shock and multiple occlusion, correlation of, (1943) 125
trauma and, (1944) 140
treatment, (1943) 125
drugs, (1943) 126
xanthine compounds, (1943) 127
- Coronci**
appointment and qualifications, (1941-2) 199
fees at inquest, (1941-2) 199
- Corpus callosum**
agenesis of, (1941-2) 174
tumours of, (1940) 230
- Corpus luteum, hormone,** (1943) 95
prevention of abortion and premature labour by, (1943) 333
- Corti, organ of**
differential stain for hair cells of, (1940) 283
localizing symptoms of disease of, (1940) 283
- Cortical lesions, hemiplegia, in,** (1943) 241
- Corticosterone, (1944) 53**
shock treated with, (1940) 529
- Cortin, (1939) 164, (1943) 94**
pneumonia treated by sodium chloride and, (1941-2) 355
pre-operative administration of, (1941-2) 387
- Corynebacterium diphtheriae**
diffusing factor and substance B, (1941-2) 209
soluseptamine and M & B 693, action of, (1941-2) 341
virulence test, (1941-2) 209
- Cosmetics**
dermatitis caused by, (1940) 258
eye injuries due to, (1940) 258
- Cotton-seed oil, substitute for olive oil,** (1940) 127
- Cotton thread, as suture material,** (1944) 15
- Cottonometer, continuous recording of cerebrospinal fluid pressure by,** (1941-2) 188
- Cough, (1943) 180**
- Cranberries, calcium retention, effect on,** (1939) 311
- Cranial nerve, (1940) 255**
affections, (1939) 294
optic chiasma, arachnoiditis affecting, (1939) 294
seventh nerve, flattening of nares in diagnosis, (1939) 294
neuritis, vitamin B₁₂ therapy, (1940) 586
- Cranio-facial dysostosis, (1943) 295**
- Craniofacialia**
meningocele, associated with, (1941-2) 396
radiological diagnosis, (1944) 233
- Craniotomy**
bifrontal, for cerebrospinal rhinorrhoea, (1941-2) 188
contra-indicated on live child, (1939) 182
- Crash helmets, (1944) 270**
value of, (1943) 250
- Crataegus oxyacantha, hypertension treated with tincture of,** (1940) 216
- Creatine metabolism, mental deficiency, in,** (1940) 407
- Creatinine**
clearance test, kidney function, of, (1940) 118
coefficient, in muscular dystrophies, (1940) 414
tolerance test, muscular dystrophies, in, (1940) 414
urinary, in mental defectives, (1940) 407

CUMULATIVE INDEX

Creolin, scabies treated with, (1940) 531
 Crohn's disease, (1939) 294; (1941-2) 199, (1943) 180
 aetiology, (1939) 294
 anaphylactic purpura simulating, (1943) 180
 clinical picture, (1941-2) 199
 infantilism as sequel, (1939) 295
 metabolism in, (1941-2) 200
 radiology, (1941-2) 199
 surgical treatment, (1943) 180
 Cross immunity, exanthematous and endemic typhus, between, (1943) 371
 Cross infection, (1941-2) 13
 streptococcal, (1943) 51, 248
 Crouzon's disease, (1943) 295
 Crush injuries (1941-2) 1
 amputation in, (1943) 249
 prolonged compression of limbs, (1941-2) 269
 renal lesions in, (1943) 249
 rupture of duodenum with fat necrosis and peritonitis, (1943) 250
 treatment, (1941-2) 269, (1943) 250
 syndrome, (1941-2) 1, 9, 269, (1944) 271
 analogy between eclamptic phenomenon and, (1944) 24
 anuria, (1944) 271
 blood pressure in, (1944) 271
 clinical picture, (1944) 271
 experimental results, (1944) 272
 impairment of renal function in, (1941-2) 269
 obstetric shock and, (1943) 19
 refrigeration, experiments with, (1944) 273
 treatment, intermittent positive pressure, (1944) 272
 (C) ryotherapy in acne, (1939) 185 (1941-2) 129
 C IAB, surgery, uses in, (1944) 321
 Cubitus valgus, (1939) 319
 Cuff test in angina pectoris, (1939) 216
 Cullen's sign of ruptured tubal pregnancy, (1939) 339
 Curare, (1939) 472
 convulsion therapy, use in, (1940) 59, 491, (1944) 346
 Curarine and eserine, antagonistic effects, (1939) 472
 Cushing's syndrome, (1939) 478
 adrenal virilism diagnosis from, (1939) 192
 Cutaneous horns, (1943) 345
 sensibility, (1943) 74
 Cutis verticis gyrata with acromegaly, (1943) 105
Cyanose tardiva, (1941-2) 248
 Cyanosis
 enterogenous, (1939) 295
 methylene blue in treatment, (1939) 295
 sulphonamides cause of, (1939) 176, 295
 sulphonamides causing, (1940) 120, 133, 457, (1941-2) 115
 Cyclobarbitone, (1944) 110
 Cycloidal sodium, hexobarbitone soluble, official name for, (1940) 127
 Cycloplegia
 action of atropine, scopolamine and homatropine-paredrine, (1940) 449
 drugs used for production of, (1940) 508
 Cyclopropane, (1939) 163
 anaesthesia by, (1939) 208
 asthma, in, (1939) 234
 clinical merits and demerits, (1944) 137
 CO₂ absorption technique, (1940) 109
 heart, effect on, (1940) 109
 labour, in, (1940) 19
 percarine anaesthesia, and, (1939) 212
 routine anaesthesia, as, (1940) 109
 Cyst
 cavum vergae, of, (1941-2) 175
 congenital, of round ligament of liver, (1940) 388
 dermoid *See also* Dermoid cyst
 nasal septum, of, (1941-2) 204
 gas, of intestine, (1941-2) 272
 larynx, of, (1940) 375, (1943) 41
 mammary, (1939) 264
 pancreatic, (1941-2) 321, (1944) 315

Cyst—continued
 pleura, of, (1940) 394
 renal, (1939) 394
 semilunar cartilages, of, (1940) 362
 Cysteine
 gonadotrophic hormones, effect on, (1940) 520
 hydrochloride, anticoagulant properties, (1940) 451
 Cysticercosis
 cerebral, difficulty of radiological detection, (1941-2) 200
 epilepsy, (1940) 255, (1941-2) 222
 Cysticercus cellulosae, incidence and detection in man, (1941-2) 200
 Cystine, effect on lactation, (1941-2) 262
 hydrochloride, infected wounds treated with, (1941-2) 268
 Cystitis, (1939) 243
 antiseptics in, (1939) 243
 benzochrome, (1939) 243
 sulphanilamide, (1939) 243, (1940) 208
 tuberculous, end-results of, (1939) 244
 Cystosarcoma phyllodes, (1943) 163
 Cystoscopy
 Hunner's ulcer of bladder, in, (1944) 94
 mercury poisoning after, (1940) 555

D

Da Costa's syndrome, (1941-2) 2, 244 *See also* Effort syndrome
 Dacryocystitis, (1939) 397
 new-born, of, treatment, (1941-2) 281
Dallia variabilis, scorpion sting treated with leaves of, (1939) 241
 Darier's disease, (1943) 181
 vitamin A therapy in, (1941-2) 200
 Dark-adaptation, prolonged, in obstructive hepatic jaundice, (1941-2) 273
 test for vitamin A deficiency, (1940) 585
 Day nurseries, (1944) 8
 Deaf
 education of, (1941-2) 52
 hearing aids for, (1939) 100
 Deaf-mutes
 aids for, (1939) 103
 mental capacity of, (1941-2) 53
 Deafness, (1939) 296, (1944) 193
 Dealness, (1939) 296, (1944) 193
 audiometric examination, (1939) 296
 aviators, in, (1940) 206, (1941-2) 160
 Beethoven's, (1941-2) 56
 cause, obvious, without, (1944) 193
 chronic, prostigmin in, (1941-2) 201
 conduction, prophylactic treatment, (1940) 256
 constitutional, oestrin in treatment of, (1939) 296
 diagnosis, (1941-2) 201, (1943) 181
 hormone therapy, (1940) 255
 lesions, effect of certain, (1941-2) 55
 Meniere's disease and, (1944) 404
 nerve, (1939) 297
 aetiology and treatment, (1939) 297
 nicotinic acid in treatment, (1939) 297
 oestrogenic substances in treatment, (1940) 255
 onset, mode of, (1941-2) 55
 otosclerosis, (1940) 255 (1941-2) 201
 surgical treatment, (1939) 298
 vitamin and calcium therapy, (1939) 297
 palistecrosis and, (1943) 181
 prevention by protection devices, (1943) 182
 prophylactic treatment, (1940) 256
 psychological
 effects of, (1941-2) 52
 reactions, (1941-2) 201
 quinine in relation to, (1939) 297
 senile, (1944) 367
 surgical treatment, (1940) 256
 treatment, (1941-2) 201, (1944) 194
 prostigmin, (1941-2) 201; (1943) 182
 methylsulphate, (1941-2) 201
 round-window grafts, (1941-2) 201
 vitamin A deficiency in relation to, (1939) 297
 vitamin B deficiency, (1939) 297
 vitamin C and D therapy, (1939) 297
 vitamin therapy, (1940) 256

CUMULATIVE INDEX

Death

sudden, in infantile eczema, (1940) 285
sudden and unexpected, common causes, (1939) 298

Débridement, (1940) 9

Decicam, (1941-2) 113

lime burns of conjunctiva, in, (1939) 289

Decurvon pectin-insulin, (1940) 267

Deficiency diseases

dietetic, (1940) 4
during present war, (1944) 9
originating in the human body, (1940) 4
progress in, (1940) 4

Degeneration

calcareous, of cornea, (1943) 180
causes of, (1939) 15
hepato-lenticular, (1943) 241

Dehydrating agent, sorbitol as, (1941-2) 339

Dehydration

blood changes in, (1941-2) 128
convulsion treated by, (1944) 185

gastroic acidity and, (1940) 437

Delinquency, medico-legal aspects of, (1944) 346

Delirium tremens

abstinence as causal factor, (1943) 110
oxygen therapy, (1940) 173
treatment of, (1939) 195
vitamin B₁, (1940) 157

Delousing, (1940) 531

Dementia

præcox. *See* Schizophrenia

pre-senile, (1941-2) 84

Demerol, spasmodic cases, effects in, (1944) 321

Demyelination

cerebral oedema cause of, (1939) 124

copper, effect of, on, (1939) 121

Denatured alcohol, hypoglycaemia due to, (1943) 110

Denervation, preganglionic, (1944) 81

Dental

disease, children, in, (1944) 196

hypoplasia, caries and, (1944) 196

sepsis, (1944) 196

complications after extraction of teeth, (1941-42) 202

gastroic disorders and, (1944) 31

neurological complications, (1941-2) 202

short-wave therapy, (1941-2) 202

systemic disease, in relation to, (1939) 298

vitamin therapy, effect on incidence, (1940) 256

Dentistry, conservative, (1944) 31

Dentists, silicosis in, (1940) 529

Dentition

abnormal, (1941-2) 207

deciduous, importance of, (1944) 197

diet in relation to, (1939) 299

disorders associated with, (1944) 198

vitamin D and, (1940) 130

Dentures, gastroic disorders, and, (1944) 31

Depression

liver function tests in, (1940) 55

suicide, safeguarding from, (1944) 76

treatment, (1940) 57, 487

cardiazol, (1940) 487

convulsion therapy, (1940) 57

haematoporphyrim, (1940) 487

shock, (1939) 118

Depressive states. *See* Psychoses, affective

Deicum's disease, (1939) 188

Dermal sinuses, intraspinal, (1943) 349

Dermatitis (1939) 229, (1941-2) 202

allergic, (1940) 163

protamine zinc insulin causing, (1943) 187

amidopyrine causing, (1940) 257

arsenical, herpes simplex associated with, (1941-42) 256

arsphenamine causing, (1941-2) 332

atrophicus maculosa, (1944) 375

9-bromo-fluorine causing, (1940) 258

carrots causing, (1941-2) 203

causes of toxic, (1940) 257-9

citrus fruits causing, (1939) 299

contact, of the feet, (1944) 198

cosmetics causing, (1939) 573, (1940) 258

dye clothing causing, (1940) 258

Dermatitis—continued

elastiglass causing, (1943) 183

ethyl mercury phosphate causing, (1941-2) 203

exfoliative, (1943) 184

fatal case, (1941-2) 204

generalized, ammoniated mercury ointment causing, (1943) 364

naphthalene causing, (1941-2) 204

phenobarbitone causing, (1941-2) 204

Ritter's disease, sulphapyridine in, (1940) 260

gangrenosa infantum, symptoms and treatment, (1939) 300

gentian violet causing, (1941-2) 203

herpetiformis, aetiology, (1939) 300

sensitization to halogens and bacterial allergens, (1941-2) 204

industrial, (1944) 373

injury and poisoning causing, (1943) 182

insecticide causing, (1940) 258

iroko wood causing, (1941-2) 203

irradiation, surgical treatment of, (1941-2) 202

lipstick causing, (1943) 183

mint causing, (1940) 259

nail lacquer and polish causing, (1941-2) 203, (1943) 183

neurotic, due to amidopyrine, (1940) 257

nicotinic acid deficiency cause of, (1939) 14

occupational,

bar-tenders, (1940) 259

coal miners, (1940) 259

fur industry, (1944) 260

prevention, (1940) 260

phenothiazine causing, (1940) 258

plants causing, (1941-2) 202

poison ivy causing, (1941-2) 203

pyrethrum causing, (1941-2) 202

radio-, surgical treatment of, (1941-2) 202

respirator, rubber, (1943) 182

smoke causing, (1944) 198

streptococcal, sulphamidamide in, (1940) 532

sulphonamide causing, (1940) 257, (1943) 183

thiocyanates causing, (1940) 257

toxic, (1939) 299, (1940) 257-9, (1941-2) 202, (1944) 198

traumatic, mental deficiency associated with, (1939) 411

triethanolamine causing, (1940) 258

vaseline causing, (1939) 299

venenata, (1941-2) 203

sulphonated oil as detergent in, (1941-2) 203

woods, irritant, causing, (1941-2) 203

Dermatofibroma, (1941-2) 393

Dermatology, (1939) 62

present-day outlook, (1939) 62

relation to general medicine, (1939) 65

Dermatomyositis, (1940) 413, (1941-2) 309, (1943) 348

compared with systemic lupus erythematosus, (1941-2) 309

complications, (1941-2) 309

metabolic disturbances in, (1941-2) 309

relation of progressive sclerodermato, (1941-2) 379

Dermatophytosis pedis, (1941-2) 233

Dermatosclerosis, (1944) 366

Deirmatoses

atopic, histamine treatment of, (1943) 112

pyogenic,

sulphanilamide in, (1940) 260

sulphonamide ointments in, (1944) 199

sulphapyridine in, (1941-2) 342

Dermoid cyst

congenital, of nasal septum, (1941-2) 204

intradiploic epidermoids, (1940) 261

intraspinal, (1943) 347

orbital, (1943) 184

ovary, of,

malignant, (1941-2) 320

traumatic rupture of, (1941-2) 319

vagina, of, obstructing labour, (1940) 373

Derobin, (1943) 94

Derris elliptica, (1941-2) 391

Derris root, scabies treated by, (1941-2) 391

Desert

fever, (1943) 146

rheumatism, (1943) 146

CUMULATIVE INDEX

Desmoid tumours
back, of, (1943) 185
histology and clinical characteristics, (1943) 184

Desoxycorticosterone, (1944) 53
Addison's disease, in, (1939) 109, 166
fibromyomas after oestrogen injections by, prevention of, (1941-2) 383

Desoxycorticosterone acetate, (1943) 94
Addison's disease treated with, (1940) 154, (1941-2) 131, (1943) 107, (1944) 53
androgenic effect of, (1940) 525
burns, in, (1940) 238
cardiac failure after, (1941-2) 132
embryo implantation, effect on, (1941-2) 335
endometrium, effect on, (1941-2) 335
foetal shock treated with, (1943) 338
incomplete syndromes after treatment with, (1943) 107
nephrosclerosis produced by, (1944) 122
oestradiol for normal infants, and, (1941-2) 335
pellets, implantation of, (1940) 155, 453
shock treated with, (1944) 371
sublingual administration, (1944) 54
Addison's disease, in, (1941-2) 131
uraemia treated with, (1941-2) 417

Dextrin-maltose-dextrose carbohydrate, use in infant feeding, (1941-2) 262

Dextrocardia, (1941-2) 246

Dextrose *See* Glucose

Diabetes insipidus, (1939) 301, (1941-2) 205, (1944) 46
aetiology, (1940) 261
alcohol tolerance, effect on, (1939) 194
diabetes mellitus, sequel of, (1939) 309, 313
hypothalamus and, (1940) 66
pituitary gland and, (1940) 66, 261
pituitary metastasis from mammary carcinoma, (1939) 301
polyuria, (1940) 66
treatment (1944) 46
pitresin tannate, (1941-2) 205
total thyroidectomy, (1941-2) 205
twins, non-identical, in, (1943) 185

Diabetes mellitus, (1939) 67, 301, (1941-2) 205, (1943) 32, 185, (1944) 197
acidosis, treatment of, (1943) 187
acromegaly associated with, (1940) 148
Addison's disease associated with, (1940) 153, (1943) 106
aetiology, (1941-2) 205, (1943) 32
unsolved problems in, (1940) 4
alcohol tolerance, effect on (1939) 195
alkalosis complicating, (1939) 309
alum-precipitated insulin, (1940) 266
aneurin administration in, (1941-2) 206
anterior pituitary extract producing, (1943) 32, 185
ascorbic acid in, (1941-2) 206
avitaminosis during insulin therapy, (1940) 265
biliary function, associated disturbances of, (1940) 263
blood sugar in, (1941-2) 207
carbohydrate and fat metabolism, (1943) 32
cataract, in, (1944) 177
children, in, (1939) 307
endocrine disorders, (1939) 307
hepatic enlargement, (1939) 307
insulin, (1940) 262
prognosis, (1940) 262
treatment, (1939) 308
clinical picture, (1940) 262, (1941-2) 205, (1943) 186
coma, (1943) 36, 187, 245
complications, (1943) 35, 187
condition of eye in, (1943) 36
prognosis, (1940) 262
sodium bicarbonate treatment of, (1939) 308
treatment, (1943) 187, (1944) 200
warning symptoms of, (1941-2) 207
complications, (1941-2) 205
decurvon pectin-insulin, (1940) 267
dextrose tolerance test, intravenous, (1940) 264
one-hour two-dose, (1940) 263
diabetes insipidus sequel of, (1939) 301, 309
diagnosis, (1940) 263, (1941-2) 206

Diabetes mellitus—*continued*
diet, (1939) 302, (1944) 199
gangrene and, (1940) 263
glycogenic hepatomegaly and, (1940) 263
haematoporphyrin, action of, (1939) 306
hepatomegaly, glycogenic, and, (1940) 263
hepatomegaly and dwarfism complicating, (1943) 35

Houssay phenomenon, (1940) 262
hypoglycaemia, (1943) 35
insulin, (1940) 265-7, (1941-2) 206
alum-precipitated, (1940) 266
avitaminosis, (1940) 265
blood-sugar and respiratory quotient, in relation to, (1939) 301
comparative merits of crystalline, regular, and zinc protamine, (1940) 266
comparison of preparations, (1943) 33, 186
complications of injections, (1939) 304
decurvon pectin, (1940) 267
local reactions, allergy in relation to, (1940) 265
peroral, (1939) 305
protamine, (1939) 67
protamine and zinc protamine, (1940) 266
protamine hexamine, (1940) 267
resistance to, (1943) 186, (1944) 200
single doses of different types, (1944) 200
subcutaneous implantation of tablets, (1939) 306
suppositories, (1940) 265
zinc globulin (1940) 267
zinc protamine, (1939) 18, 68, 303, (1940) 265, (1941-2) 206
allergic dermatitis after, in, (1943) 187
local reactions, (1940) 265
soluble insulin, and, (1940) 266
intercapillary glomerulo-sclerosis and, (1941-2) 152
jaundice, latent, in, (1940) 263
ketosis associated with, (1940) 113
kidneys in, (1943) 288
labour and, (1944) 201
lactation, effect on, (1944) 201
legs, lesions of, (1940) 263
lipodystrophia with, (1940) 263
menopause, complicating, (1941-2) 191
nephrotic syndrome with hypertension in, (1941-2) 205
pancreatitis, acute haemorrhagic, complicated by, (1941-2) 321
pathogenesis, (1944) 199
pellagra-like condition in, (1941-2) 206
peptic ulcer associated with, (1939) 301
pituitary, anti-diabetogenic principle, (1941-2) 205
diabetogenic principle, (1943) 332
extract, effect of, (1940) 264
substances, anterior, effect of, (1944) 199
pregnancy, (1939) 308, (1941-2) 16, (1944) 201
pre-operative procedure in, (1941-2) 207
prognosis, (1939) 306
progress in, (1944) 201
pulmonary tuberculosis complicating, (1939) 308
retinal haemorrhages in, (1943) 186
schizophrenia associated with, (1943) 317
surgery, (1939) 306
symmetrical peripheral neuropathy in, (1941-2) 206
treatment, (1940) 264-8, (1941-2) 206, (1943) 33, 186
aneurin and riboflavine, (1941-2) 206
ascorbic acid, (1941-2) 206
complications, (1940) 268, (1943) 187
diet, new scheme of, (1944) 199
insulin quinine, (1941-2) 207
insulins, new, (1943) 33
clear protamine zinc, (1943) 34
globin (zinc), (1943) 34
hexamine, (1943) 34
histone zinc, (1943) 34
irradiation of pituitary and adrenal glands, (1943) 152
oestrin, (1943) 34
oral administration, (1943) 33

CUMULATIVE INDEX

- Diabetes mellitus continued*
treatment continued
 pre-operative procedure, (1941-2) 207
 thiamin, (1941-2) 422
 unsolved problems, (1940) 4
 zinc protamine insulin, (1941-2) 206
 tuberculosis associated with, (1941-2) 205
 zinc protamine insulin in, (1941-2) 206
 urinary and blood sugars, relation between, (1939) 302
 Van den Bergh test in, (1940) 263
 vitamin A deficiency in, (1940) 268
 vitamin B₁ deficiency in, (1941-2) 422
 vitamin C nutrition in, (1941-2) 425
 vitamin therapy, (1941-2) 206
 Wesselow and Griffiths's test, (1941-2) 206
 xanthomatosis and lipodystrophia with, (1940) 263
- Diabetic*
 coma, warning symptoms of, (1941-2) 207
 retinitis, varices in, (1941-2) 376
- Diabetogenic principle of anterior pituitary gland,* (1943) 332
- Dial, prolonged narcosis by paraldehyde and,* (1940) 418
- Diamidine compounds,* (1944) 322
 protozoal infections, in, (1941-2) 100
 trypanosomiasis treated with, (1944) 391
- Diamidinostilbene,* (1943) 5
 4-4-diamidinostilbene, kala-azar treated with, (1940) 362, (1941-2) 274
 trypanosomiasis treated with, (1941-2) 413
- Diaphragm disease,* (1939) 309
 congenital hernia, clinical picture of, (1939) 309
 hernia, (1940) 268, (1943) 293
 clinical picture, (1940) 268
 surgical treatment, (1940) 268
 lipoma, (1940) 268
 paralysis, one-sided, in infancy, (1943) 290
 paroxysmal flutter of, (1941-2) 207
 rhabdomyosarcoma, (1939) 310
 tumours, (1940) 268
 wounds and injuries, X-ray examination in, (1943) 322
- Diarrhoea*
 acute, treatment by sulphathiazole, (1943) 188
 flagellate infection and, (1939) 310, (1940) 269, (1941-2) 208, (1944) 202
Giardia intestinalis infection and, (1939) 310, (1940) 269, (1941-2) 208
 treatment with atabrin dithydrochloride, (1941-1942) 208
Giardia lamblia infestation associated with, (1944) 202
 in infancy and childhood. *See* Diarrhoea, infantile
 infantile, (1939) 310, (1940) 270, (1941-2) 208
 bacteriology, (1944) 203
 biochemistry, (1941-2) 208
 epidemics, sources of infection in, (1944) 203
 new-born, in, (1940) 270
 pectin-agar mixtures in, (1940) 270
 prevention of, (1939) 278
 summer, (1940) 270
 treatment, (1940) 270, (1944) 204
 apple and tea treatment, (1939) 310
 banana preparations, (1941-2) 209
 lyophilic plasma and sulphathiazole, (1943) 188
 sulphathiazole, (1941-2) 208
 vitamin C excretion in, (1941-2) 208
 treatment,
 apple diet, (1940) 269
 vitamin deficiency diseases due to chronic, (1941-1942) 208
 war-time, in, (1944) 210
- Diastase, low blood,* (1941-2) 163
- Diathane hydrochloride for urethral anaesthesia,* (1939) 209
- Diathermy,* (1939) 26
 angiomatosis retinae treated by catholysis and, (1941-2) 377
 testicular function, effect on, (1940) 543
 toxic goitre, in, (1939) 354
- Diathesis, psoriatic,* (1944) 338
- Dick test, reliability of,* (1941-2) 261
- Dicoumarin,* (1944) 117
 prothrombin, effect on, (1944) 322
- Dienoestrol,* (1943) 98, (1944) 110
- Diet*
 abortion, relation to, (1944) 22
 Addison's disease, in, (1939) 191
 adiposity, in, (1939) 189
 amino-acids in, (1941-2) 232
 anaemias of pregnancy, in, (1940) 187
 anaesthesia, before, (1940) 110
 banana as supplementary, (1940) 270
 calcium in, (1941-2) 232
 calculus, relation to, (1940) 366
 cancer and, (1940) 240
 carbohydrate, in pulmonary tuberculosis, (1941-1942) 293
 cirrhosis of liver, role in, (1940) 387
 cranberries, calcium retention, effect on, (1939) 311
 dentition, in relation to, (1939) 299
 diabetes, in, (1939) 302
 diabetes mellitus, in, (1944) 199
 disseminated sclerosis, in, (1943) 196
 fasting, (1939) 311
 gastric acidity, in, (1943) 245
 gout, in, (1944) 244
 haemoglobin level and, (1944) 131
 hepatic cirrhosis, in, (1943) 268
 high fat, cirrhosis of liver and, (1944) 290
 role in gout, (1940) 321
 high protein, in pulmonary tuberculosis, (1944) 293
 hypertension, in, (1943) 151
 infancy and childhood, in, (1939) 381
 liver injury modified by, (1940) 549
 low fat, high carbohydrate, in gout, (1944) 244
 Meniere's syndrome, in, (1940) 584
 Meulengracht's, (1943) 300
 minerals, need for certain, (1944) 132
 minimum optimum requirements, (1941-2) 232
 peptic ulcer, in, (1941-2) 328
 pre-anaesthetic, (1940) 110
 pregnancy, in, (1940) 187, (1944) 22
 lactation, and, in, (1939) 29, 220
 puerperium, and, in, (1944) 142, 5
 toxemia, in, (1940) 480
 prematurity and (1944) 22
 prenatal, and breast feeding, (1944) 261
 skin disease in relation to, (1939) 65
 still-birth, relation to, (1944) 22
 toxemia of pregnancy, relation to, (1944) 22
 treatment, in, (1939) 311
 vitamins in, (1943) 187, 213
 war-time, (1943) 214, 16
 wholemeal bread, (1943) 213
 winter, in, (1943) 216
- Dietetic deficiency,* (1940) 271, (1941-2) 209
- dental,*
 development and, (1944) 196
 hypoplasia and caries and, (1944) 196
 diarrhoea, chronic, causing, (1941-2) 208
 incidence in California, (1944) 204
 neuritis, multiple, in, (1940) 424
 pregnancy, in, (1944) 142, 5
 syndromes due to, (1943) 189
- Dietetic deficiency diseases,* (1939) 311
 dermatological manifestations of hypovitaminosis, (1939) 311
 recent progress in, (1939) 13
- Dietetics*
 progress in, (1940) 4
 surgery, in, (1939) 24
- Diethyl ether, anaesthesia,* (1940) 109
- Diethylstilboestrol,* (1943) 336, (1944) 49 *See also* Hormones, sex
 action of, (1940) 522
 leucoplakia, kraurosis and senile vaginitis treated with, (1944) 27
 uses of, (1939) 35, 110
 vaginitis, post-menopausal, treated with, (1941-2) 429
 vulvo-vaginitis treated with, (1940) 319
- Digestive disorders in soldiers,* (1940) 25, (1943) 198, (1944) 214 *See also* Effort syndrome and Peptic ulcer

CUMULATIVE INDEX

- Digilanid**
heart, effect on, (1941-2) 334
heart failure, in, (1939) 371
- Digitalis**
action of, (1940) 337
auricular
fibrillation, in, (1940) 192
standstill caused by, (1940) 192
clinical assay of, (1940) 338
heart-block, in, (1940) 191
heart failure, in, (1939) 60, 371, (1944) 250
treated with ouabain and, (1941-2) 254
lanata, (1941-2) 334, 337
purpurea, (1941-2) 334, 337
- Digoxin**
heart disease, in, (1940) 135
heart failure, in, (1939) 60
- Dihydriotachysterol**
hypoparathyroidism treated with, (1940) 432, (1944) 47
pemphigus vulgaris treated with, (1941-2) 324
tetany, post-operative, treated with, (1939) 291, (1940) 433
thyroid and parathyroid deficiency treated with, (1940) 589
- Dihydroxyanthranol**, (1943) 94
- Dilantin**
sodium *See also* Sodium diphenylhydantoinate
poisoning by, (1941-2) 409
soluble, (1941-2) 113
- Dimitrophenol medication**, cataract formation, in relation to, (1939) 188
- Diodone**, (1944) 110 *See also* Diodrast
solution of, (1943) 96
- Diodrast** *See also* Perabrodil
anaphylaxis, and, (1943) 321
death after intravenous administration, (1944) 355
pulmonary embolism, use in diagnosis of, (1944) 296
- Diospyrobezoar**, stomach, in, (1940) 546
- Diphenan**, (1943) 94
- Diphtheria**, (1939) 312, (1941-2) 209 (1943) 49, 55, 190
advance in prevention and treatment of, (1939) 41
advances in diagnosis of, (1939) 78
albuminuria, importance of, (1939) 312
antitoxic serum, analysis of, (1941-2) 260
antitoxin,
"anti-B" factor in (1941-2) 209
leprosy treated with, (1940) 381
level in pregnancy, (1941-2) 260
therapy, (1939) 313
bacteriology, (1939) 312
pathology, and, (1941-2) 209
carriers, treatment by sulphathiazole snuff, (1943) 171
circulatory failure, electrocardiographic observations, (1944) 205
culture media, comparative values of, (1940) 272
cutaneous scratch test, (1939) 313
diagnosis, (1940) 272, (1941-2) 66
formol toxoid in treatment of leprosy, (1941-2) 284
glandular fever simulating, (1941-2) 235
heart in, (1940) 271
immunization, (1940) 272, (1941-2) 4, (1943) 55, 190, 192
adults, in, (1943) 190
alum-precipitated toxoid, (1943) 191
propaganda for, (1943) 190
results of, (1943) 191
tetanus, against, and, (1941-2) 260
malignant, blood transfusion in, (1943) 30
mortality, (1943) 190
paralysis, vitamin B₁ in, (1940) 129
pathology, (1940) 271
potassium tellurite test, (1939) 312, (1940) 272
present war, during, (1944) 10
prophylaxis, (1941-2) 66
Schick test, (1940) 272
bullous reactions, (1941-2) 209
serum therapy in, (1940) 3
specific prophylaxis for, (1939) 76
toxin, effect on heart, (1940) 271
- Diphtheria—continued**
toxoid, leprosy treated with, (1940) 381
toxoid injection, end-results of, (1941-2) 210
treatment, (1941-2) 66
antitoxin, (1941-2) 209
vitamin B₁, (1941-2) 210
umbilicus, of, (1940) 572
vagina, of, (1941-2) 429
viability and air-borne infection, (1941-2) 209
virulence test, (1941-2) 209
- Diplacusis**, (1940) 283
- Dipsomania**, hypnosis treatment in, (1939) 378
- Disease**, psychological aspects of, (1940) 7
- Disinfection**, (1943) 52
aerosols and gaseous chemicals, (1944) 41
ultra-violet irradiation, (1943) 53, 105, (1944) 42
- Dislocations**, (1940) 273-7, (1941-2) 210, (1943) 193
convulsion therapy causing, (1940) 491
elbow joint, treatment of, (1940) 277
fractures, fracture-dislocations and associated injuries, (1939) 314
delayed calcification and atrophy of bones, hydrochloric acid treatment of, (1939) 314
hip, treatment of dislocation of, (1939) 314
injuries, gross, with fracture of joints, (1939) 315
os calcis, fractures of, (1939) 315
temporo-mandibular luxation, treatment of, (1939) 314
tibia and fibula, treatment of fractures of upper end of, (1939) 315
radius, head of, fracture of ulna associated with, (1940) 276
- Disproportion**, induction of labour in (1944) 280
- Disseminated**
encephalitis, disseminated sclerosis, diagnosis from, (1939) 316
hamartiosis, (1943) 264
sclerosis, (1939) 316, (1940) 277-9
aetiology, (1940) 277
allergy and, (1940) 277
blood coagulation time in, (1944) 207
clinical picture, (1944) 207
course and prognosis, (1939) 316
dietetic and related studies in, (1943) 196
disseminated encephalo-myelitis, diagnosis from, (1939) 316
heredity, (1940) 277
neuralgia, trigeminal, in, (1940) 278
pathogenesis, (1944) 207
treatment, (1940) 278
artificial fever, by, (1941-2) 212
lecithin, (1940) 278
nicotinic acid and vitamin B₁, (1940) 278
- Distemper**, canine, (1940) 4
- Dithranol**, (1943) 94
- Diuretics**
mercurial,
cardiac dropsy, in, (1940) 337
cardiac oedema, in, (1943) 1
fatalities, investigation of, (1944) 323
heart failure, in, (1941-2) 253
nephrosis, in, (1943) 290
oedema in, (1940) 5
poisoning by, (1944) 385
sucrose and other solutions, (1940) 455
renal changes, (1940) 455
- Diverticulitis**, (1941-2) 212
colo-vesical fistula and, (1941-2) 25
obstruction and colostomy, (1941-2) 212
proctoscopy in diagnosis, (1944) 207
- Diverticulosis and diverticulitis**, (1939) 316, (1941-1942) 25, 212
aetiology, (1939) 316
clinical picture, (1939) 317
duodenal diverticulum, (1939) 317
duodeno-jejunal diverticula, (1939) 317
gall-bladder, of, (1943) 218
prognosis, (1939) 318
radiological diagnosis, (1939) 318
- Diverticulum**
bladder, of, (1944) 156
malignant papilloma in, (1943) 145

CUMULATIVE INDEX

- Diverticulum—continued**
 duodenum, of, (1941-2) 212
 pharyngeal, (1943) 309
 stomach, of, (1941-2) 402, (1943) 354
 Divinyl ether, anaesthesia, (1940) 109
 Dmelcos, chancroid, in, (1940) 91
 Doderlein's bacillus
 hydrogen ion concentration of vagina, effect on, (1940) 22
 leucorrhoea, in, (1940) 19
 Dolantol, (1941-2) 113
 Dolantin, (1941-2) 113
 Doryl
 action and composition of, (1939) 164-6
 carbachol, official name for, (1940) 127
 Drainage, appendicectomy, after, (1940) 190
 Dressings, Cellophane, (1940) 349
 petroleum jelly, (1941-2) 264
 tulle gras, (1941-2) 263
 Dropsy, cardiac, mercurial diuretics and urea in, (1940) 337
 Drowning, resuscitation, (1941-2) 212
Drug
 addiction, (1939) 318, (1940) 279, (1943) 196, (1944) 208
 abstinence symptoms, (1944) 208
 forms of, (1940) 279
 marijuana or hashish, (1939) 318
 war-time, in, (1940) 280
 eruptions, (1939) 319, (1941-2) 213
 arsphenamines, purpura haemorrhagica due to, (1941-2) 213
 bromide causing, (1941-2) 213
 insecticide causing, (1940) 280
 magnesium silicate causing, (1944) 208
 mercurial, (1939) 319
 purpura haemorrhagica due to arsphenamines, (1941-2) 213
 sulphanilamide causing, (1939) 319
 sulphapyridine causing, (1941-2) 213
 sulphonamides causing, (1943) 183
 intoxications, (1939) 13
 therapy, recent developments in, (1941-2) 111, (1944) 109
Drugs, (1940) 127-37, 444-63, (1943) 93 See also
 Chemotherapy
 action of, (1940) 444
 age, weight and dosage, relation between, (1940) 444
 antipyretic, (1941-2) 339
British Pharmaceutical Code (Third and Fourth Supplements), (1943) 93
British Pharmacopoeia
 Fourth Addendum, (1941-2) 112
 Fifth Addendum, 1942, (1943) 93
 economy in, (1941-2) 111
 emulsion, application in, (1940) 444
 German origin, substances of, (1941-2) 112
 injections, (1941-2) 112
 modern, some, (1939) 163
 acetylcholine, (1939) 164
 Addison's disease, in, (1939) 166
 aluminium hydroxide, (1939) 167
 amyl nitrite, (1939) 165
 amytal, (1939) 163
 anacardone, (1939) 164
 anaesthetics, medullary and vascular stimulants, (1939) 163
 antacids, (1939) 167
 atropine methylnitrate (eumydrin), (1939) 165
 avertin, (1939) 163
 barbiturates, (1939) 163
 benzedrine, (1939) 164
 cardiazol, (1939) 164
 coramine, (1939) 164
 cortin, (1939) 164
 cyclopropane, (1939) 163
 desoxycorticosterone, (1939) 166
 doryl, (1939) 164
 ephedrine, (1939) 164
 ethylene, (1939) 163
 eucortone, (1939) 164
 eupaverin, (1939) 165
 evipan, (1939) 163
 familial periodic paralysis, in, (1939) 166
Drugs—continued
 modern, some—continued
 glyceryl trinitrate (nitroglycerin), (1939) 165
 hypnotics, sedatives and anaesthetics, (1939) 163
 magnesium trisilicate, (1939) 168
 mechoyl, (1939) 166
 metrazol, (1939) 164
 muscular weakness, drugs acting on, (1939) 166
 myasthenia gravis, in, (1939) 166
 nembutal, (1939) 163
 papaverine, (1939) 165
 pentothal, (1939) 163
 phenobarbitone sodium, (1939) 163
 physostigmine, (1939) 164
 picROTOXIN, (1939) 164
 pitressin, (1939) 165
 pituitary extract, posterior lobe, (1939) 164
 plain muscle, drugs acting on, (1939) 164
 prostigmin, (1939) 165
 sympatol, (1939) 164
 Thomsen's disease, in, (1939) 166
 ventol, (1939) 164
 names,
 officially approved, (1944) 109
 proprietary, (1940) 127, (1941-2) 113
 recently approved, (1944) 110
 nasal mucosa, action on, (1940) 445, (1941-2) 331
 National War Formulary, (1941-2) 112
 new official substances, (1941-2) 112
 nose, for, (1941-2) 334
 Pharmacy and Medicines Act 1941, (1941-2) 111
 prescribing in war-time, (1943) 5, 82, 93
 recent developments, (1940) 127-37, (1944) 109
 rectal administration of, (1941-2) 339, (1944) 327
 reduction of heat by, (1941-2) 339
 shortage and the war, (1941-2) 111
 skin, action on, (1941-2) 331
 sterilization methods, (1941-2) 113
 substitutes for foreign, (1940) 127
 sympathomimetic and parasympathomimetic, (1941-2) 346
 war and supplies of, (1940) 127
 Ductless glands See Endocrine glands
 Ductus arteriosus, patent, (1941-2) 2
 infected, treatment by sulphapyridine and ligation, (1943) 233
 left ventricular compensation, (1941-2) 247
 ligation of, (1943) 14
 S. viridans infection, relief of, after ligation of, (1944) 368
 surgical treatment, (1941-2) 247
 Dunkirk, evacuation from, (1944) 5
Duodenal
 atresia, congenital, (1941-2) 272
 contents, optimum hydrogen-ion concentration, (1944) 263
 ulcer, (1941-2) 326 See also Peptic ulcer
 aetiology and treatment of, unsolved problems in, (1940) 5
 incidence relative to gastric ulcer, (1944) 31
 perforation of, (1940) 12
 after bismuth sulphate meal, (1940) 438
 new physical sign, (1940) 438
 soldiers, in, (1940) 25
 treatment, partial gastrectomy, (1941-2) 326
 tuberculous, perforation of, (1941-2) 326
Duodentis, radiological findings in, (1943) 321
Duodenum
 atresia, (1943) 253
 carcinoma, (1940) 355
 primary, (1943) 254
 congenital, (1941-2) 272, (1944) 233
 diverticulum of, (1939) 317
 peri-vaterian, (1941-2) 212
 ileus of, (1939) 388
 leiomyosarcoma of, (1939) 388, (1940) 355
 obstruction of, congenital, (1943) 253
 sprue, in, (1941-2) 27
 traumatic rupture of, (1943) 250
 ulcer,
 treatment of, (1939) 46
 tuberculous, perforation of, (1941-2) 326
 Dupuytren's contraction, microscopic investigation, (1941-2) 213

CUMULATIVE INDEX

Dust
bacteria in, (1943) 53
diphtheria bacilli in, (1941-2) 209
house, allergens in, (1944) 125
Dust-borne organisms, in hospital wards, (1941-2) 185
Dwarfism
aetiology, (1940) 281
hepatomegaly complicating diabetes mellitus, and, (1943) 35
hormone treatment, (1943) 197
infantilism, and, (1939) 319, (1940) 281, (1943) 197, (1944) 208
antuitrin growth hormone in relation to, (1939) 108
infantilism with webbing and cubitus valgus, (1939) 319
pituitary and thyroxine, in, (1940) 281
Dys
burns treated with, (1940) 236-9
dermatitis due to dyed clothing, (1940) 258
Dying, euthanasia, voluntary, (1940) 281
Dyschezia, treatment, (1944) 191
Dyschondroplasia, (1944) 162
dysostosis multiplex, (1940) 224
Dyscyesis, (1939) 158
Dysentery
amoebic, skin manifestations of, (1941-2) 138
treatment, (1940) 136, (1943) 114
acetarsol, (1940) 136
carbarsone, (1940) 136
emetine, (1940) 136
bacillary, (1939) 320, (1944) 209
calcium and kaolin, (1939) 320
classification of bacilli, (1940) 78
clinical types, (1944) 209
culture media, new, (1944) 37
diagnosis,
faecal and serological examinations, (1944) 209
laboratory, (1944) 209
Flexner infections, (1944) 209
incidence, (1944) 37
laboratory investigations, (1944) 37
pectin and metal pectinates in, (1939) 320
prophylaxis, (1944) 210
treatment,
hypertonic saline transfusions, (1944) 100
succinylsulphathiazole, (1944) 210
sulphaguanidine, (1944) 101, 209
sulphanilicguanidine, (1941-2) 65, 213 (1943) 85, 99
sulphapyridine, (1941-2) 118
sulphathiazole, (1943) 188
war, in, (1940) 78, (1944) 210
diagnosis, (1941-2) 64
recent work on, (1944) 61
treatment, (1941-2) 65
sulphonamides in, (1941-2) 65
Dysgerminoma, in pseudo-hermaphrodites, (1943) 294
ovary, of, (1940) 428
Dysidrosis, (1939) 320
hidradenitis suppurativa, (1939) 320
Dyskeratoid dermatosis, (1943) 181
Dyskinesia, biliary, X-ray appearance in, (1941-2) 233
Dysmenorrhoea, (1939) 321, (1941-2) 214, (1944) 211
aetiology, (1941-2) 214, (1944) 211
androgens, importance of, (1944) 211
hormone therapy, (1940) 132, 282, (1944) 52
insulin therapy, (1939) 321
male sex-hormone in relation to, (1939) 35
oestradiol benzoate in, (1940) 282
oestrogenic substances in blood tested for, (1939) 321
progesterone, implantation of, (1941-2) 384
sex hormones, (1944) 211
spasmodic, oestrogens in treatment, (1944) 26
testosterone propionate, (1940) 282
treatment, (1940) 132, 282, (1944) 212-14
benzedrine sulphate, (1941-2) 214
hormone, (1944) 211
oestrogen, (1944) 26, 211
thyroid, (1939) 321
uterine contractions and, (1941-2) 214

Dysostosis
hereditary cranio-facial, (1943) 295
multiplex (typus Hurler), (1940) 224, (1943) 220
Dyspepsia, (1941-2) 4, (1944) 216
carbohydrate intestinal, (1944) 216
aetiology, (1944) 216
air swallowing in, (1944) 216
clinical manifestations, (1944) 216
flatulence in, (1944) 217
cutaneous abdominal hyperaesthesia in, (1941-2) 215
differential diagnosis, (1939) 321, (1941-2) 215
Forces, incidence in the, (1940) 25, (1941-2) 214, (1943) 2, 198, (1944) 214. *See also* Floit syndrome and Peptic ulcer
gastroscopic findings, (1944) 222
functional, (1944) 30, 214, 340
gastroscopy, (1944) 222
diagnosis of, in, (1939) 48
nervous, (1944) 215
organic, symptoms suggesting, (1944) 214
present-day aspects of, (1944) 215
radiological diagnosis, (1941-2) 215
Dysphagia
causes, (1940) 282 (1944) 218
hysterical, (1940) 146
Plummer-Vinson syndrome in, (1940) 146
sideropenic, (1941-2) 128
upper, with anaemia (Paterison's syndrome), (1939) 43
vitamin B deficiency causing, (1940) 282
Dysphonia, spastic, (1944) 219
Dyspnoea, (1939) 322
coal miners, in, (1939) 322
sighing, (1939) 322
vitamin B₁ therapy in, (1941-2) 254
Dys-symbioly, (1940) 489
Dystrophy
adiposo-genital, (1940) 152
muscular. *See* Muscular dystrophy
vitamin B₁ therapy, (1941-2) 428
vitamin E therapy (1941-2) 5, 426, 428

F

Fat
aero-otitis media, (1940) 49
anatomy, (1944) 193
aviators' disabilities incident to, (1940) 48
cholesteatomas of, (1943) 199
diseases, (1939) 86, 322 (1940) 283-5 (1941-2) 52, 216, (1943) 38, 198, (1944) 219. *See also* Deafness
actinomycosis, (1939) 323
aviators, in, (1943) 141
cerebellar abscess due to, (1943) 162
chemotherapy in, (1941-2) 56
diagnosis, (1940) 283
facial palsy, (1939) 88
intra-cranial complications, (1939) 87
Lempert's technique, (1939) 325
mastoidectomy, (1939) 325
mastoiditis, (1943) 198
sulphanilamide treatment of, (1939) 324
neurological conditions associated with, (1939) 322
otitis media,
acute, (1939) 323
chronic, (1939) 324
otogenic meningitis, treatment of, (1939) 325
otosclerosis, (1939) 87
transmastoid drainage, (1939) 325
drum, blue, (1943) 198
explosions, effect of, (1940) 47
external auditory meatus injuries, (1940) 46
fractures of skull involving, (1940) 49, 53
fungal infection of, (1940) 284
gunshot wounds, (1940) 48
haemorrhage, caused by aneurysm of internal carotid (1941-2), 144
head injuries involving, (1940) 49-53
infections, hydrocephalus following, (1940) 345
middle. *See* Middle ear
noises in, (1944) 193, 195

CUMULATIVE INDEX

Ear—continued

- pinna injuries, (1940) 46
- protruding, plastic correction of, (1943) 212
- skull fractures involving, (1940) 49-53
- tympenic membrane rupture, (1940) 46
- Eating utensils, bacterial contamination of, (1944) 42
- Eclampsia
 - cerebral venous thrombosis and, (1940) 67
 - hypertension and, (1941-2) 18
 - 'late', (1943) 4
 - placental ischaemia and, (1944) 24
 - pre-eclamptic toxæmia, placental ischaemia and, (1944) 24
 - prevention of, (1944) 334
 - renal damage, permanent, following, (1940) 17
 - renal lesion in, (1944) 24
 - renin and, (1941-2) 18
 - vitrum viride therapy, (1941-2) 358
- Ecthyma contagiosum, (1941-2) 217
- Ectodermal dysplasia, familial incidence, (1941-2) 147
- Ectopia vesicæ, treatment of, (1940) 14
- Eczema, (1939) 63, 326, (1940) 285
 - aetiology, (1939) 63
 - allergic, and cataract, (1941-2) 137
 - arm, extensor surfaces of, (1939) 326
 - children, in, treatment of, (1939) 198
 - infantile, (1941-2) 137
 - sudden death in, (1940) 285
 - sulphathiazole ointment in, (1943) 199
 - vitamin B therapy, (1940) 285
- Edentulous patients, gastric carcinoma in, (1944) 31
- Effort, angina of. See Angina pectoris
- Effort syndrome, (1940) 329-31, (1941-2) 2, 46, 244, (1943) 62, 231, (1944) 340
 - aetiology, (1941-2) 244
 - clinical picture, (1941-2) 244
 - fatigue, tests of, in, (1943) 232
 - general review, (1941-2) 244
 - history and terminology, (1943) 231
 - personality types and, (1941-2) 245
- Effusion, chylous, (1943) 276
- Ehlers-Danlos syndrome, (1939) 340 (1940) 301, (1941-2) 230, (1943) 212
- Eighth nerve, affections of, (1941-2) 199
- Elastiglass, dermatitis due to, (1943) 183
- Elbow
 - dislocations and their treatment, (1940) 276
- Electrical
 - anaesthesia, (1940) 110
 - convulsion therapy in mental disease, (1940) 59, 494, (1941-2) 80, 218, 368, (1943) 4, 66, (1944) 73
 - amylal as prognostic test, (1944) 74
 - brain, effect on, (1944) 74
 - electroencephalogram in, (1944) 74
 - psychoses, in, (1944) 351
 - risks, (1944) 73
 - schizophrenia, in, (1944) 349
 - current, cataract caused by, (1940) 243
 - injury, (1943) 10, 199
 - clinical effects of, (1941-2) 217
- Electrocardiogram
 - Adams-Stokes attacks and, (1941-2) 246
 - diphtheria, in, (1944) 205
 - effects of fear on, (1941-2) 149
 - gunshot wound of heart, in, (1943) 236
 - heart disease, congenital, in, (1943) 233
 - hypertension, in, (1941-2) 245
 - induced fever, in, (1943) 131
 - interpretation of records, (1944) 248
 - method of detection not all revealing, a, (1943) 131
 - multiple chest-lead, in pulmonary embolism, (1941-2) 296
 - posture effect of, (1944) 247
 - strophantin and glucose, effects of, (1941-2) 340
 - T-wave inversion, (1941-2) 245
 - tachycardia, paroxysmal, in, (1944) 150.
 - Wolff-Parkinson-White syndrome, (1943) 131
- Electrocardiograph in angina pectoris, (1939) 215
- Electrocardiography, (1939) 59, (1940) 5
- Electrocardiograms, human, (1943) 77

Electroencephalogram

- electrical convulsion therapy, in, (1944) 74
- epilepsy and cerebral tumours, in, (1939) 124
- psychopathic individuals, in, (1944) 79
- Electroencephalography, (1943) 65
 - diagnosis of cerebral tumour, in, (1941-2) 175
 - epilepsy, in, (1939) 124, (1941-2) 91, (1944) 226, 229
- Electrolysis, wounds treated by, (1943) 249
- Electrolyte balance, surgical shock, in, (1940) 527
- Electrolytes, blood, and menstrual cycle, (1941-2) 163
- Electrosurgery, gall-bladder, of, (1940) 306
- Electrotherapy, (1939) 326, (1941-2) 217
 - aconitine iontophoresis in rheumatism, (1939) 326
 - direct current, (1941-2) 217
 - high frequency currents, (1941-2) 217
 - ionization, (1941-2) 217
 - low voltage varying currents, (1941-2) 218
 - magnetism, importance of, (1941-2) 217
 - paralysed muscles, of, (1943) 77
 - short-wave therapy, rotating electrode in, (1939) 326
- Elephantiasis, (1940) 398
 - clitoris, of, (1941-2) 430
 - glycerin injections in, (1939) 421
 - penis and scrotum, of, (1941-2) 325
 - treatment of, (1939) 340
- Embolectomy, (1941-2) 218
- Embolism
 - abdominal aorta, of, (1943) 125
 - air,
 - artificial pneumothorax causing, (1943) 128
 - complicating blood transfusion, (1943) 28
 - high-altitude flying, in, (1943) 6, 140
 - arterial, (1941-2) 218
 - embolectomy, (1941-2) 218
 - heparin in treatment, (1940) 286
 - mural thrombi as source of, (1941-2) 218
 - prevention of gangrene of extremity, (1941-2) 218
 - arteries of extremities blocked by, (1944) 83
 - cerebral fat, triazol convulsant therapy causing, (1941-2) 368
 - dicumarin as prophylactic, (1944) 322
 - fat, (1941-2) 1, 74
 - cerebral, (1943) 337
 - complicating fractures, (1940) 274
 - pulmonary, (1943) 2
 - respiratory symptoms and radiological findings, (1943) 337
 - shock and, (1941-2) 386
 - triazol convulsant therapy causing, (1941-2) 368
 - mesenteric, (1941-2) 125
 - pneumothorax caused by, (1941-2) 290
 - post-operative, prevention of, (1944) 322
 - pulmonary, (1941-2) 74
 - amniotic fluid causing, (1943) 261
 - causes and prevention of, (1944) 15
 - diagnosis, (1940) 395
 - multiple lead cardiograms, by, (1941-2), 296
 - heparin in treatment, (1940) 395, (1941-2) 296
 - incidence and occurrence, (1941-2) 295
 - ligation of femoral veins for prevention, (1941-2) 296
 - obstetrics and gynaecology, in, (1944) 280
 - operative prevention, (1941-2) 296
 - phlebitis and, (1943) 375
 - post-operative, (1941-2) 295
 - predisposing conditions, (1941-2) 295
 - radiographic diagnosis, use of diodrast, (1944) 296
 - treatment, (1941-2) 296
- Embryo
 - implantation, effect of desoxycorticosterone acetate, (1941-2) 335
 - respiration in foetal sheep, (1944) 330
- Embryonic extract, wounds, use in, (1940) 351
- Embryotomy, (1941-2) 279
- Emergency Medical Service, (1944) 3
 - ambulance services, (1944) 5
 - central organization, (1944) 4
 - early months of the war, (1944) 5
 - evacuation from Dunkirk, (1944) 5

CUMULATIVE INDEX

- Emergency Medical Service—continued**
 evacuation scheme, (1944) 6
 first-aid posts, (1944) 5
 laboratories, (1944) 5
 organization and operation, (1944) 3
 period of intensive air-raids, (1944) 5
 planning and development, (1944) 4
 provision for
 civil patients, (1944) 4
 military sick and casualties, (1944) 4
 regional organization, (1944) 4
 subsequent developments, (1944) 5
- Emetine, amoebic dysentery, in, (1940) 136**
Emotion syndrome, (1944) 340, 341
Emotional disturbance, schizophrenia, in, (1944) 347
Emotions, effect on stomach, (1944) 30
Emphysema
 mediastinal, (1944) 301
 pulmonary, (1939) 327
 bullous, advanced, (1944) 220
 chest, form of, in, (1941-2) 219
 chronic obstructive, (1941-2) 219
 cor pulmonale, relation to, (1943) 240
 functional impairment and, (1941-2) 219
 tuberculous obstructive, in children, (1941-2) 219
- Empyema**
 acute,
 Br. abortus infection causing, (1940) 286
 operative treatment of, (1941-2) 219
 pyogenic non-tuberculous, scoliosis following, (1940) 539
 tuberculous, sulphapyridine in, (1940) 286
 treatment, (1944) 220
 drainage, (1944) 220
 thoracoplasty, (1944) 220
- Emulsion**
 antiseptic, wounds treated by, (1943) 248
 drugs, application of, in, (1940) 444
- Encephalitic diseases, classification of, (1943) 200**
Encephalitis
 arsenical, (1944) 25
 chicken-pox complicated by, (1943) 173
 haemorrhagic, arsphenamine causing, (1944) 221
 haemorrhagic superior, (1940) 69, 287
 herpes zoster complicated by, (1939) 374
 measles complicated by, (1941-2) 302, (1944) 298, 301
 whooping-cough complicating, (1940) 594
- Encephalitis epidemica, (1939) 327, (1941-2) 219**
 chronic stage, (1944) 221
 classification of encephalitic diseases, (1943) 200
 differentiation of viruses, (1941-2) 220
 electro-surgical excision of premotor cortex, (1943) 200
 intranuclear inclusion bodies in nerve cells, (1943) 200
- Parkinsonism and psychosis,**
 benzedrine sulphate in, (1940) 287
 treatment of, (1944) 221
 syntropan, with, (1941-2) 220
 post-encephalitic Parkinsonism, Bulgarian bella-donna in, (1939) 327
 treatment, (1944) 221
 g-erythroidine hydrochloride, (1941-2) 332
 syntropan, with, (1941-2) 220
 virus, (1944) 221
- Encephalogram**
 diagnostic value of, (1944) 89
- Encephalography, (1940) 102, (1944) 165**
 diagnosis of cerebral tumour, in, (1941-2) 175
 epilepsy, therapeutic effect on, (1940) 295
 headache, in, (1940) 103
 head injuries, in, (1944) 357
 nicotinic acid deficiency causing, (1940) 271
 pentothal sodium anaesthesia for, (1940) 178
- Encephalo-myelitis, (1939) 328**
 acute disseminated, (1941-2) 220
 new conceptions and allied forms, (1941-2) 220
 toxoplasma causing, (1941-2) 220
 arsphenamine causing, (1944) 221
 measles and, (1939) 328; (1944) 298, 301
 post-vaccinal meningo-encephalo-myelitis, (1943) 201
- Encephalo-myelitis—continued**
 spontaneous, (1939) 329
 vaccination, after, (1939) 328
- Encephalopathy**
 arsphenamine causing, (1941-2) 332, (1944) 221
 burns causing, (1941-2) 178
 lead, (1943) 263
 children, in, (1941-2) 282
 inhalation causing, (1944) 387
 simulating cerebral tumour, (1941-2) 282
 sulphamethylthiazole therapy causing, (1941-2) 175
 toxic,
 arsphenamine causing, (1944) 221
- Encopresis, children, in, (1943) 314**
Enderteritis, arteriosclerotic, sympathectomy for, (1944) 151
Enderteritis obliterans, hydrotherapy in, (1939) 377
Endocarditis
 atypical verrucous, (1941-2) 250
 combined with lupus erythematosus, (1941-2) 250
 bacterial, treatment, sulphonamides, (1939) 171, (1941-2) 118
 erysipelothrix causing, (1940) 334
 gonococcal septicaemia associated with, (1941-2) 237
Haemophilus para-influenzae causing, (1940) 334
 infective, heparin in, (1940) 137
 malignant, (1940) 334-6, (1941-2) 249, (1943) 236
 subacute monilial, (1944) 250
 malignant subacute, (1940) 334 6
 bacterial and morbid anatomy, (1944) 249
 bacteriology, (1940) 334
 fever therapy and sulphanilamide, (1940) 335
 heparin in, (1940) 336
 sulphonamide compounds, (1940) 334
 treatment, (1940) 334 6
 meningococcal, (1941-2) 250
 monilial, (1944) 250
 pneumococcal, (1944) 249
 rheumatic, (1943) 327
Streptococcus viridans infection, (1941-2) 250
 subacute bacterial, (1941-2) 2, 249, (1943) 237, (1944) 249
 aetiology, (1941-2) 249, (1944) 249
 bacteriology and morbid anatomy, (1941-2) 251, (1943) 237
 clinical picture, (1941-2) 250
 meningococcal infection without meningitis, (1941-2) 250
 micrococci, atypical, causing, (1944) 249
 nervous system, effects on, (1941-2) 250
 pneumococci causing, (1944) 249
Staphylococcus albus causing, (1943) 237
Streptococcus viridans infection
 recovery, with, (1941-2) 250
 treatment, (1941-2) 251
 syphilitic aortic valvulitis, after, (1941-2) 249
 treatment, (1941-2) 251
 chemotherapy, (1943) 237
 heparin, (1941-2) 251, (1943) 237
 review of, (1943) 237
 sulphapyridine, (1941-2) 251
 sulphapyridine and heparin, (1940) 336; (1941-2) 251
 sulphonamides, (1943) 237, (1944) 249
 syphilitic, (1941-2) 249
- Endocervicitis**
 treatment,
 carbon dioxide, solid, in, (1940) 289
 coagulation and ionization, (1940) 288
 novocain injection, (1940) 289
- Endocrine**
 diseases, (1939) 14
 disorders,
 acne vulgaris, association with, (1943) 104
 differential diagnosis by radiography, (1944) 357
 skin disease associated with, (1939) 65
 sprue, association with, (1940) 542
 X-ray examination in, (1944) 357
- glands,**
 advances in knowledge of, (1940) 4
 anencephaly in relation to, (1939) 341
 homosexuality, male, and, (1940) 60, 527

CUMULATIVE INDEX

- Endocrine—*continued*
glands—*continued*
 mental disease and, (1940) 55
 tumours, hormonal effects, (1940) 231
 therapy. *See* Hormone therapy
 acne, in, (1939) 186
 Dercum's disease, in, (1939) 188
 survey of, (1939) 17
Endocrines, pharmacological aspects, (1939) 108
desoxycorticosterone, subcutaneous implantation of, (1939) 109
 ethyl testosterone or pregnenolone, (1939) 110
 pituitary, anterior lobe of, (1939) 108
 synthetic oestrogens, (1939) 110
Endocrinology, (1941-2) 4
 advances in, (1940) 4, (1944) 44
 nervous diseases, and, (1940) 6
 survey of, (1939) 34
Endometrial
 biopsy, ovulation, test for, (1944) 26
 extract, (1941-2) 383
 mole-type tumours, (1940) 577
 transplants, lungs in, (1941-2) 221
Endometriosis, (1941-2) 221
 carcinoma of cervix, associated with, (1941-2) 419
 clinical aspects, (1940) 288
 endometrial transplants in lungs, (1941-2) 221
 morbid anatomy and pathogenesis, (1941-2) 221
 post-operation scars in, (1943) 201
 recto-vaginal septum, of, (1941-2) 221
 treatment by testosterone propionate, (1941-2) 221
Endometriosis and adenomyoma, (1939) 329
 arm, endometriosis of, (1939) 329
 ovary, endometriosis of, (1939) 329
 umbilicus, endometriosis of, (1939) 329
Endometritis, chronic, (1943) 201
Endometrium
 bleeding, normal, types of, (1943) 19
 desoxycorticosterone acetate, effect of, (1941-2) 335
 hyperplasia, progesterone therapy, (1940) 288
 pregnancy, changes in, (1940) 477
 senile changes in, (1943) 201
Endoscopy, (1943) 202
 myeloscope, (1940) 67
 peroral, pentothal sodium in, (1943) 121
 surgery, in, (1939) 24
 urinary tract, of, (1939) 330
 cystoscopy, anaesthesia in, (1939) 330
 leprosy, treatment of, in, (1941-2) 284
Endotoxoid
 Grasset's tubercle,
 lupus vulgaris treated with, (1941-2) 300
Enema
 barium, in intussusception, (1940) 353
 nutrient, (1944) 327
Entamoeba histolytica
 amoebiasis cutis caused by, (1941-2) 138
 rectum, in, (1940) 167
Enteric fevers, (1940) 289-91; (1941-2) 221, (1944) 37, 222
 advances in diagnosis of, (1939) 78
 combined immunization against tetanus and, (1941-2) 407
 diagnosis, (1941-2) 63
 B. typhosus in, (1941-2) 63
 epidemiology, (1944) 60
 newer aspects of, (1944) 224
 present war, during, (1944) 11
 prophylaxis, (1941-2) 64
 vaccines, (1944) 222
 recent work on, (1944) 60
 specific prophylaxis for, (1939) 76
 sulphonamides in, (1939) 330
 T.A.B.C vaccine in, (1941-2) 261
 treatment, (1941-2) 63
 mandelic acid, with, (1943) 202
 vi-antigen in, (1939) 380
Enteritis
 infective,
 epidemiology, (1944) 59
 recent work on, (1944) 59
 newly-born, in, (1940) 270
Enterobiasis, children, in, (1941-2) 312
Enterobius vermicularis, (1941-2) 312
Enterocolitis, ulcerative, phenolphthalein test in, (1941-2) 273
Enterogastrone, peptic ulcer treated by, (1943) 301
Enuresis treatment
 hypnosis, by, (1939) 378
 urethral dilatation, by, (1943) 202
Envelopes, Bunyan-Stannard, in treatment of burns, (1941-2) 114, 180
Enzyme
 nerve cell, of, (1943) 74
 proteolytic, in treatment of ganglion, (1941-2) 243
 respiratory, (1940) 129
Eosinophil
 counts in asthma, (1939) 231
 leukaemia, in children, (1943) 265
Eosinophilia
 allergic conditions, in, (1940) 203
 asthma, (1939) 231
 periarteritis nodosa and, (1940) 203
 periarteritis nodosa, in, (1939) 224
 pneumonia, in, (1940) 468
 pulmonary, (1941-2) 157
 tuberculous pleuritic effusion, in, (1941-2) 291
Epanutin, (1941-2) 113; (1943) 95 *See also* Sodium diphenylhydantoinate
 epilepsy treated with, (1940) 135
Ephedrine, (1939) 164
 action of, (1939) 164-6
 asthma, in, (1939) 200
 children, after-effects in, (1943) 302
 intranasal use of, (1943) 302
 myasthenia gravis treated with adrenaline and, (1943) 285
 nasal spray, in, (1939) 285
Ephynal, (1940) 130 *See also* Vitamin E
Epicondylitis of humerus, (1940) 300
Epicutan, wounds, use in, (1940) 351
Epidemic
 diseases, (1943) 48, 84 *See also* Infectious fevers
 myositis, (1943) 5
 i epidemics resulting from wars, (1940) 75
Epidemiology, present war, (1941-2) 62
Epidermoid, intradiploic, (1940) 261
 intraspinal, (1943) 349
Epidermolysis bullosa, (1940) 533
 cancer of throat associated with, (1944) 225
 familial incidence, (1944) 225
Epidermophytosis, (1940) 304
Epithidymis tumours
 adenomatous, (1943) 203
 myomatous, (1943) 203
 primary malignant, (1943) 203
Epithidymitis
 acute, (1944) 226
 trauma causing, (1940) 291
 non-gonococcal and non-tuberculous, (1944) 226
 non-specific, (1944) 19
Epidual abscess, diagnosis of, (1941-2) 397
Epilation, (1940) 328
Epilepsy, (1939) 331, (1941-2) 222; (1944) 226
 aetiology, (1939) 331, (1940) 291, (1941-2) 222; (1944) 226
 benign hyperplasia of gums in, (1941-2) 222
 blood, specific gravity of, (1944) 226
 brilliant vital red, (1939) 333; (1940) 291
 cardiazol,
 diagnosis, in, (1939) 332
 treatment, in, (1939) 333
 children, in, treatment, (1940) 295
 convulsant toxins, (1939) 331
 convulsion therapy, (1944) 229
 convulsions, (1944) 228
 cysticercosis and, (1940) 255
 cerebral, and, (1941-2) 200, 222
 diagnosis,
 differential, (1944) 227
 positive water balance test, (1944) 228
 diphenylhydantoinate in, (1939) 126
 electroencephalography in, (1941-2) 91; (1944) 226, 229
 encephalography, in, (1940) 295
 feigned, in war-time, (1940) 400
 focal, surgical treatment of, (1939) 333
 haemato-encephalic barrier, (1940) 291
 heredity, (1939) 331

CUMULATIVE INDEX

Epilepsy—continued

- idiopathic, (1944) 228
- mental abnormalities in, (1944) 227
- mentality, effect of phenobarbitone, (1940) 293
- myoclonus, (1939) 333
 - primary optic atrophy, associated with, (1940) 295
- physiological disturbance, (1939) 331
- prevention, (1944) 229
- recent work on, (1944) 230
- seizure patterns, (1944) 228
- survey of, (1939) 124
- time relationship of attacks, (1939) 332
- traumatic, (1944) 226
- treatment of, (1939) 19; (1940) 135, 291–5; (1944) 229
 - azosulphamide, anticonvulsant action of, (1943) 203
 - children, in, (1941–2) 222
 - convulsion therapy, (1944) 229
 - encephalography, (1940) 295
 - pancreatic extract, insulin-free, (1940) 294
 - phemitone, (1940) 135
 - phenobarbitone, (1940) 293
 - belladonna, and, (1939) 332, (1941–2) 222
 - prominal, (1940) 294
 - pyridine, (1944) 229
 - sodium diphenylhydantoinate, (1940) 135, 291, 293, (1941–2) 222, (1944) 230
 - hemiplegia due to, (1940) 293
 - vitamin C deficiency in, (1941–2) 222
- voltage changes, (1944) 228
- water balance in, (1944) 226, 228, 230
- water balance test, (1944) 228
- water metabolism in relation to, (1944) 226
- water retention, (1939) 331
- whooping-cough, complicating, (1940) 594
- Epileptiform attacks, hypoglycaemic shock, complicating, (1940) 494
- Epiroia, (1943) 204. *See also* Tuberosus sclerosis
 - bone changes in, (1940) 295
 - nature of, (1944) 231
- Epinephrine *See* Adrenaline
- Epiphyses, diseases and injuries, (1939) 334, (1940) 296
 - chondro-epiphysitis, hypothyroidism as cause of, (1939) 334
- Epiphysitis
 - regeneration of centres of ossification, (1940) 296
- spine, of, (1940) 296
- Epistaxis, (1939) 334
 - spontaneous haemorrhage into maxillary sinus, (1939) 334
- Epithelioma
 - multiple benign cystic, (1941–2) 393
 - pancreas, of, (1940) 432
 - Paterson's syndrome predisposing to, (1939) 43
 - vulva, of, (1941–2) 430
- Epituberculosis, differential diagnosis from Löffler's syndrome, (1941–2) 157
- Eptoin, (1941–2) 113, (1943) 95
- Equilibrium, tests for, in diagnosis of intracranial tumours, (1939) 95
- Ergometrine, (1939) 473
 - normal puerperium, in treatment of, (1941–2) 370
- Ergosterol
 - intoxication, (1943) 377
 - irradiated, (1940) 130. *See also* Vitamin D
- Ergot
 - alkaloids, thyrotoxicosis treated with, (1941–2) 236
 - involution of post-partum uterus, effect in promoting, (1944) 23
 - labour, induction of, with, (1940) 374
 - toxic effects, (1940) 451
- Ergotamine, thyrotoxicosis treated with, (1941–2) 236
- Ergotamine tartrate
 - cardiac manifestations following injection of, (1940) 409
 - migraine treated with, (1939) 20; (1940) 409
 - toxic effects, (1940) 451
- Ergotoxine, scorpion toxin, antidote to, (1940) 448
- thyrotoxicosis treated with, (1941–2) 236
- Erspamer's pre-enterochrome cells, (1944) 359

Eruptions

- achromia flava amycotica, (1939) 334
- anomalous and atypical, (1939) 334; (1941–2) 223
- rheumatism, acute, in, (1940) 511
- urticate lesions, (1939) 334
- Erysipelas
 - prognosis, (1940) 297
 - sulphanilamide in, (1940) 297; (1941–2) 224
 - sulphonamides in, (1939) 17, 335
- Erysipelothrix rhusiopathiae*, endocarditis due to, (1940) 334
- Frythema, (1941–2) 224
 - clinical picture, (1941–2) 224
 - external causes, due to, (1941–2) 224
 - internal causes, due to, (1941–2) 224
 - livedo reticularis, (1941–2) 224
 - multiforme, (1941–2) 224
 - nodosum, (1939) 335
 - allergy suggested as cause of, (1939) 336
 - radiological intrathoracic appearances in, (1943) 205
 - sarcoidosis, relation to, (1943) 205
 - tuberculosis, associated with, (1939) 335, (1941–2) 224
- palmar hereditarium, (1943) 205
- scarlatiniforme, (1941–2) 224
- T.A.B. vaccine causing, (1943) 282
- Erythema and purpura, (1939) 64
- Erythraemia, (1939) 336
 - blood pressure in, (1944) 231
 - circulatory adjustments in, (1941–2) 225
 - clinical picture, (1941–2) 225
 - complications, (1944) 231
 - coronary occlusion and, (1944) 231
 - hepatic and splenic complications, (1944) 231
 - high altitudes cause of, (1939) 336
 - hypertension in, (1944) 231
 - intracranial tumour complicating, (1944) 231
 - leukaemoid reaction in, (1944) 231
 - lungs, (1940) 297
 - radiological diagnosis, (1943) 206
 - stem-celled sarcoma, associated with, (1939) 336
 - thrombosis complicating, (1941–2) 225
 - treatment,
 - lipocac and choline, (1941–2) 225
 - vitamin C and sodium bicarbonate, (1941–2) 225
- Erythroblastæmia, (1940) 172, (1941–2) 141
- Erythroblastic
 - anaemia, (1941–2) 140
 - leukaemia, (1943) 265
- Erythroblastosis, (1941–2) 140
 - foetalis, (1943) 3, 16, 24
 - Rhesus factor, (1943) 3, 16, 24, 29, 148
 - transfusion accidents and, (1943) 119
 - treatment, vitamin K, (1943) 230
 - with intra-uterine death, (1943) 119
 - vitamin K therapy, (1941–2) 141
- Erythrocyanosis, (1941–2) 226
 - clinical picture, (1941–2) 226
 - treatment, (1941–2) 226
- Erythrocytes, (1940) 4. *See also* Blood cells, diseases of
- Erythromelalgia, (1941–2) 226
 - treatment of, (1939) 337
- Erythrophagocytic anaemia, (1941–2) 140
- Eschatin, shock treated with, (1940) 528
- Eserine, myasthenia gravis treated with, (1943) 284
- Esidrone, (1943) 1
- Esthiomène, (1940) 91
- Ether
 - anaesthesia,
 - bulk ether, use of, (1940) 175
 - carbon dioxide absorber, (1944) 135
 - convulsions, (1940) 111, 174, (1943) 120
 - labour, in, (1940) 19
 - pulmonary complications, (1940) 108
 - herpetic keratitis treated with, (1943) 179
 - Ethinyl testosterone (pregneninolone), (1939) 110
 - Ethisterone, (1943) 95
- Ethyl
 - alcohol, poisoning by, (1940) 158
 - mercury phosphate, dermatitis caused by, (1941–2) 203
 - n-propyl ether anaesthesia, (1940) 175

CUMULATIVE INDEX

- Ethylene, (1939) 163
 Eucortone, (1939) 164, (1943) 94
 Eumydrin (atropine methylnitrate)
 congenital pyloric stenosis, in, (1939) 165
 hypertrophic pyloric stenosis treated with, (1939) 509, (1941-2) 370
 pyloric stenosis treated with, (1940) 502, (1941-2) 4, 13, 50
 Eunuchism
 hormone therapy, (1944) 49
 testosterone and testosterone propionate, treatment with, (1941-2) 384
 Eunuchoidism, hormone therapy, (1944) 50
 Eupaverrin
 colic, in, (1939) 165
 intermittent claudication, in, (1939) 20
 pulmonary circulation, effects on, (1940) 451
 Eustachian tube
 atmospheric pressure, effect of, (1940) 48
 aviators, disabilities of, (1940) 48
 food or mucous obstruction complicating mastoiditis in infants, (1943) 198
 obstruction, vertigo caused by, (1943) 376
 physiology of, (1940) 48
 Euthanasia, voluntary, (1940) 281
 Evacuation scheme, (1944) 6
 medical and health services, (1944) 6
 nurseries and camps, (1944) 6
 refugees, (1944) 6
 school children, (1944) 6
 Eventration, (1941-2) 255
 Evil disease of Egypt, (1943) 300
 Evipan, (1939) 163
 anaesthesia, (1943) 121
 neuroses, investigation of, by, (1941-2) 259
 labour, in, (1941-2) 280
 sodium *See* Hexobarbitone soluble
 hexobarbitone soluble, official name for, (1940) 127
 narcosis in tetanus, (1941-2) 407
 rectal administration in, (1940) 375
 Evisceration, obstetric, (1941-2) 279
 Lwing's tumour of bone, (1943) 161
 Exanthem, generalized, following X-ray irradiation, (1940) 505
 Exanthemata and diphtheria, (1939) 74
 advances in diagnosis and treatment, (1939) 78
 factors determining occurrence, (1939) 74
 specific prophylaxis, (1939) 76
 Exercise
 dangers of, in old age, (1943) 331
 tolerance test, (1941-2) 44, 244
 Exercises
 graduated post-operative, effect on incidence of fatal pulmonary embolism, (1939) 33
 passive vascular, (1940) 196
 Exertion, collapse during, (1940) 205
 Exhaustion, aviators, in, (1943) 141
 Exhibitionism, (1943) 206
 Exomphalos, treatment of, (1940) 14
 Exophthalmic ophthalmoplegia, (1941-2) 319
 Exophthalmos, toxic goitre, in, (1940) 316
 Exotoxins, bacterial, (1940) 3
 Expectorants
 ammonium salts as, (1941-2) 178
 potassium iodide and ipecacuanha, relative value of, (1940) 453
 Explosions, ear, effects on, (1940) 47
 Explosives, high, lesions caused by, (1940) 9
 Extradural abscess *See* Abscess
 Extrasystole
 children, in, (1939) 223
 treatment, potassium chloride, (1941-2) 150
 Extremities
 arterial diseases, (1941-2) 151
 arteries, acute embolic occlusion, (1944) 83
 thrombosis of, (1943) 134
 upper, sympathetic innervation of, (1944) 82
 vascular diseases, (1941-2) 151
 Eye
 arboflavinosis, in, (1940) 587
 burns, (1943) 79
 diabetic coma, in, (1943) 36
 diseases, (1943) 79
 chemotherapy by iontophoresis in, (1944) 220
 Eye—continued
 diseases—continued
 focal infection in, (1944) 367, 368
 night-blindness, (1943) 80, 206
 psychoneurotic factor in, (1944) 340
 silver terrihaemoglobin in, (1941-2) 339
 sulphonamides in, (1944) 328
 treatment,
 chemotherapy, (1943) 81, 179
 epidemic gonorrhoeal ophthalmia, of, (1943) 178
 keratitis, of, (1943) 179
 recent advances, (1943) 146
 vitamins, (1943) 80
 examination of, (1939) 337, (1941-2) 226, (1944) 232
 anisokonia, (1939) 337
 atropine, dangers of, (1944) 232
 cornea, (1941-2) 226
 fundus, (1941-2) 227
 ophthalmoscopy, (1944) 232
 piedrine, use of, (1939) 337
 posterior chamber irrigation, (1939) 338
 filariasis, (1944) 233
 foreign bodies, (1943) 79
 gas poisoning, (1940) 311
 hyperemesis gravidarum and, (1943) 17
 inclusion conjunctivitis, (1943) 178
 sulphonamides in, (1944) 328
 infections,
 treatment, oligoseptic, (1940) 445
 injuries, (1943) 79
 broken spectacle glass, (1940) 253
 mustard-gas lesions, (1940) 311, (1943) 80, 220
 tetanus after, (1944) 383
 mesodermal angioma of, (1943) 205
 pain, retrobulbar injection of procaine for, (1941-2) 244
 penetrating wounds, (1944) 158
 percarine, sensitivity to, (1941-2) 338
 retinal haemorrhage, (1943) 326
 rhinosporidiosis, lesions in, (1940) 512
 steel particles in, (1944) 158
 strain, (1944) 259
 sulphanilamide, presence in, (1940) 459
 sulphonamides in, (1941-2) 118, 342
 temporo-parietal lesions affecting, (1939) 256
 tuberous sclerosis, in, (1943) 204
 tumours, (1943) 147, 326
 vitamin B₂ complex and, (1940) 587
 vitamins, effects of, (1944) 405
 wounds, (1944) 158
 Wuchereria bancrofti infestation, (1944) 233
 Eyeball injury, cephalic tetanus following, (1943) 361
 Eyelashes, injury from cosmetics, (1940) 258
 Eyelid, dermatological applications, (1944) 232
 diseases, (1940) 298
 inflammation, (1941-2) 227 *See also* Blepharitis
 injuries and diseases, (1939) 338, (1941-2) 227
 molluscum contagiosum, (1940) 298
 mycetoma, (1940) 298
 Schwannoma, (1940) 298
 tumours, (1940) 298, (1943) 207
 warts, (1939) 338
 F
 Face
 nodular syphilide of, (1941-2) 403
 powder, removal of, (1941-2) 334
 wounds, primary suture of, (1940) 348
 Facial nerve, abnormal facial movements following injury, (1940) 255
 paralysis, with cephalic tetanus, (1943) 361
 Facial palsy, (1939) 88
 nerve grafting for, (1939) 89
 Facial paralysis, herpes zoster and, (1941-2) 256
 otitis media complicated by, (1944) 219
 Facies in rheumatoid arthritis, (1943) 136
 Factory workers
 industrial poisoning,
 toluene intoxication, (1943) 364
 trinitrotoluene, by, (1943) 365
 viscose rayon industry, in, (1943) 365
 industrial psychiatry, (1943) 69

CUMULATIVE INDEX

Factory workers—*continued*

- mass radiography in, (1943) 320
- Workmen's Compensation, (1943) 69
- Faecal incontinence, children, in, (1943) 314
- Faeces
 - calcium bilirubinate and cholesterol in, (1940) 306
 - hemicellulose hydrogels, effect of, (1944) 190
 - poliomyelitis, toxic factor in, (1941) 2) 356
 - soiling of perianal skin by, (1941) 2) 147
 - urobilin excretion and blood destruction, (1944) 303
- Faints in blood donors, (1943) 31
- Fallopian tube
 - carcinoma,
 - diagnosis, (1941-2) 228
 - origin in uterus, (1941-2) 228
 - primary, (1941) 2) 228
 - treatment, (1941-2) 320
 - diseases, (1939) 338, (1941-2) 228, (1943) 207
 - actinomycosis, (1939) 339
 - blastomycosis, (1939) 339
 - Cullen's sign, (1939) 339
 - gangrene of hydatid of Morgagni, (1939) 340
 - torsion in virgin, (1939) 338
 - tubal pregnancy, (1939) 339
 - infection and ectopic pregnancy, (1941-2) 228
 - insufflation of, (1940) 22, 544
 - sterility, in, (1941-2) 399
 - non-patency, (1940) 298
 - sterilization by ligation of, (1940) 23
 - tumours, (1941-2) 228
- Familial incidence
 - cerebellar angioma, (1943) 127
 - choleco-athetosis, paroxysmal, (1941) 2) 159
 - ectodermal dysplasia, congenital, (1941-2) 147
 - epidermolysis bullosa, (1944) 225
 - haemolytic anaemia, (1941-2) 139
 - haemorrhagic telangiectasia, (1941) 2) 223
 - hepato-lenticular degeneration, (1943) 241
 - jaundice, non-haemolytic, (1941-2) 141
 - Kayser-Fleischer ring, (1943) 241
 - oedema of legs, persistent, (1941) 2) 318
 - oesophagus, short, (1940) 428
 - periodic paralysis, associated with hyperthyroidism, (1943) 298
 - periodic paralysis, treatment of, (1939) 166
 - polypoid of colon, (1944) 184
 - purpura simplex, (1941) 2) 241
- Faradic shock therapy
 - alcoholism, in, (1943) 111
 - mania, acute, in, (1941) 2) 365
 - mental disorders, in, (1941) 2) 218, 368
- Fascial sutures, hernia, for, (1940) 340
- Fasciola hepatica*, removed from common bile-duct, (1941-2) 230
- Fascioliasis, treatment of, (1941-2) 230
- Fasciolopsiasis, *Fasciolopsis buski* causing, (1943) 211
- Fasting
 - scarlet fever, in, (1940) 515
 - treatment, in, (1939) 311
- Fat
 - absorption, mechanics of, (1941-2) 26
 - carbohydrate metabolism, and, (1943) 32
 - cirrhosis of liver, relation to, (1944) 290
 - embolism, (1941-2) 1, 74
 - cerebral, (1943) 337
 - complicating fractures, (1940) 274
 - pulmonary, (1943) 2
 - respiratory symptoms and radiological findings, (1943) 337
 - shock and, (1941-2) 386
 - triazol convulsant therapy causing, (1941-2) 368
 - gout, role of high fat diet in, (1940) 321
 - lymphatic glands in, (1941-2) 300
 - metabolism,
 - faecal urobilin excretion and blood destruction, (1944) 303
 - lipotropic factors, (1943) 35
 - skin diseases, in, (1944) 375
 - necrosis, traumatic rupture of duodenum with, (1943) 250
- Fatigue
 - aviators, in, (1941-2) 35; (1943) 141
 - industry, in, (1944) 259

Fatigue—*continued*

- muscular, effect of amino-acetic acid and gelatin on, (1941-2) 331
- ophthalmic strain, (1944) 259
- tests of, (1943) 232
- war neurosis and, (1940) 62
- Fatty acids, essential unsaturated, common cold treated by, (1941) 2) 193
- Fear, effects on electrocardiogram, (1941-2) 149
- Felix's vi-serum and M & B 693 in enteric fevers, (1939) 330
- Felty's syndrome, (1944) 152
- Feminism, hyperfunction of adrenal cortex, in, (1941-2) 133
- Femoral
 - artery, pseudo-thrombotic occlusion, (1940) 195
 - vein, ligature of,
 - amputation, in, (1940) 395
 - prevention of embolism, in, (1944) 15
 - prevention of pulmonary embolism, in, (1941-2) 296
- Femur
 - fracture of, (1941) 2) 14, (1943) 195
 - neck,
 - convulsion therapy causing, (1941-2) 366
 - non-union, (1940) 274
 - treatment, (1944) 20
- Fenestrac parietales symmetricae, (1940) 224
- Fertility, seminal findings, relation to, (1940) 543
- Fever
 - abortion caused by, (1944) 120
 - blackwater, (1943) 83, 144
 - induced, electrocardiographic findings in, (1943) 131
 - infections. *See* Infectious fevers
 - initial symptom of renal tumour, as, (1941-2) 277
 - neurogenic, (1944) 346
 - relapsing, (1943) 325
 - rheumatic, (1943) 327
 - specific, encephalo-myelitis complicating, (1943) 201
 - therapy. *See* Pyretotherapy
 - gonorrhoea, in, (1939) 358
 - typhus, (1943) 84
- Fibrillation
 - auricular. *See also* Auricular fibrillation
 - muscular, peripheral origin, (1941-2) 229
 - ventricular. *See* Ventricular fibrillation
- Fibrin suture, repair of divided nerves by, (1944) 311
- Fibroblasts, interaction with leucocytes and macrophages, (1940) 569
- Fibroma
 - larynx, of, (1943) 40
 - nasopharynx, of, (1941) 2) 317
- Fibromyoma
 - prevention after oestrogen injections, (1941-2) 383
 - uterus, irradiational treatment, (1941-2) 419
- Fibrosis, hepato-lenal, (1941-2) 398
- Fibrositis, (1941-2) 229
 - aetiology, (1943) 208
 - clinical picture, (1940) 299
 - cold and wet as factors in, (1943) 208
 - diagnosis by novocain injections, (1943) 208
 - diagnosis and differential diagnosis, (1941) 2) 229
 - miners, incidence in, (1943) 208
 - panniculitis in, (1943) 208
 - review of, (1943) 210
 - treatment, (1941-2) 229, (1943) 209, (1944) 232
 - Forces, in, (1943) 209
 - heat and Scott's dressing, (1941) 2) 229
 - injection of local anaesthetic, (1941-2) 229
 - novocain injections, with, (1940) 7
 - procaine, (1943) 209
 - vitamin E, (1941-2) 230
 - unsolved problem of, (1940) 7
- Filder's myocarditis, (1943) 235
- Filaria, (1939) 340
 - breast, of, (1943) 211
 - distribution, (1944) 233
 - East Africa, in, (1944) 233
 - eye, of, (1944) 233
 - filarial elephantiasis, bandaging treatment of, (1939) 340
 - onchocercinae, arthritis caused by, (1939) 340

CUMULATIVE INDEX

- Filter-passing viruses, (1940) 4
- Finger
 agnosia, (1943) 76
 clubbed. *See* Clubbed fingers
 reflex, in diagnosis of pyramidal tract lesions, (1940) 508
- First aid
 essentials of, (1944) 271
- First-aid posts, (1944) 5
- Fistula
 arteriovenous,
 congenital, (1940) 301
 diagnosis of, (1941-2) 421
 treatment of, (1941-2) 422
 colo-vesical, and diverticulitis, (1941-2) 25
 gastro-colic, (1941-2) 329
 gastro-jejuno-colic, (1941-2) 329
 jejuno-colic, nutritional oedema due to, (1941-2) 318
 oro-maxillary, treatment of, (1944) 304
 pancreatic, (1944) 315
 sigmoido-vesical, carcinomatosis, (1944) 184
 umbilical, (1943) 371
 vesico-vaginal, operation for, (1941-2) 430
- Flagellate infections, diarrhoea associated with, (1940) 269, (1941-2) 208, (1944) 202
- Flat-foot, congenital, diagnosis and treatment, (1944) 236
- Flatulence, (1944) 216
 causes, (1944) 217
 clinical manifestations, (1944) 216
 gastric, (1944) 217
 intestinal, (1944) 217
 war and, (1944) 216
- Flavines, as antiseptics, (1944) 13
- Flexner bacillus infections, hospital outbreak of, (1944) 209
- 'Flit', dermatitis caused by, (1940) 280
- Flocculation test, Meinicke, in tuberculosis, (1941-1942) 414
- Floors, oiled, and control of infection, (1943) 53
- Floraquin, *Trichomonas vaginalis*, (1940) 382
- Flour, national, (1944) 22
- Fluid
 forcing, danger of, (1940) 301
 intramuscular injection of, (1940) 348
 overloading, effects of, by, (1944) 322
 toxæmias of pregnancy treated with, (1940) 480
- Fluke infections, intestinal, (1941-2) 230; (1943) 211
- Fluorescein, corneal examination, in, (1941-2) 227
- Fluorescent screen, foreign bodies, localization of, (1944) 355
- Fluorides
 industrial hazard, (1944) 386
 poisoning by, (1940) 560, (1944) 386
- Fluorine
 geological distribution in relation to endemic goitre, (1941-2) 235
 poisoning, osteosclerosis in, (1940) 560
- Flying *See also* Aviation
 anoxæmia, (1943) 140
 anoxia, (1943) 139
 aptitude for, (1941-2) 29
 aptitude test, (1941-2) 29
 cardiovascular stability, (1941-2) 30
 effect of altitude changes on intracranial volume, (1941-2) 160
 hearing, effect on, (1943) 141
 high-altitude, fitness for, (1941-2) 30
 hyperventilation, (1941-2) 159, (1943) 140
 night-vision, (1941-2) 30
 pre-selection of men for, (1941-2) 29
 psychological pre-selection of personnel, (1941-2) 32
 stereoscopic vision, (1941-2) 31
- Focal infection *See* Infection, focal
- Focal sepsis, in aetiology of rheumatoid arthritis, (1940) 7
- Foetal
 mortality, (1944) 351
 respiration, (1939) 31
 shock, desoxycorticosterone acetate in treatment, (1943) 338
- Foetus, (1941-2) 230
 abnormalities, (1940) 301; (1941-2) 230
 digestive system, (1941-2) 230
 genito-urinary system, (1941-2) 230
 skin, (1941-2) 230
 anonychia, partial, with bony changes, (1941-2) 230
 arachnodactyly, (1940) 301
 arteriovenous fistula, congenital, (1940) 301
 ascites, obstructed labour due to, (1941-2) 279
 asphyxia, narcosis and, (1940) 19
 bile-ducts, congenital obliteration of, (1941-2) 231
 circulation of, (1943) 15
 colon, triplication of, (1941-2) 231
 death of, causal factors, (1944) 351
 digestive system, (1944) 233
 diseases, (1940) 301, (1944) 233
 Ehlers-Danlos syndrome, (1940) 301; (1941-2) 230
 malformations and monstrosities, and, (1939) 340, (1943) 212, (1944) 233. *See also* Frythroblastosis foetalis
 anencephaly, endocrine glands in relation to, (1939) 341
 Ehlers-Danlos syndrome, (1939) 340
 nose, congenital occlusion of posterior choanae, treatment of, (1939) 341
 genito-urinary system, (1944) 234
 maternal diet and health of, (1944) 144
 maternal nutrition and, (1944) 22
 monorchia, (1941-2) 231
 nutritional requirements, (1944) 143
 respiration of, (1940) 19, (1944) 330
 respiratory system, (1944) 234
 skeleton, (1944) 233
 skull, congenital abnormality of, (1944) 233
 testis, absence of, (1941-2) 231
- Follicular hormone, Fallopian tubes, non-patency of, treated with, (1940) 298
- Folliculin
 milk secretion, action on, (1939) 220
 possible carcinogenic action of, (1939) 220
- Folliculitis naris perforans, (1939) 449
- Food, (1939) 341, (1940) 5, 254, 301, (1941-2) 231; (1943) 212, (1944) 235 *See also* Diet
 allergy, interstitial keratitis, in, (1940) 254
 calcium, (1941-2) 232
 caloric value, (1944) 235
 excessive craving for, in children, (1943) 314
 industrial workers, of, (1944) 235
 inorganic elements, (1944) 235
 iron excretion by intestine, (1939) 341
 minimum optimum requirements, (1941-2) 232
 nitrogenous constituents, (1941-2) 232
 peptic ulcer, bleeding, in cases of, (1940) 5
 poisoning, (1941-2) 232
 magnesium trisilicate in, (1939) 378
 recent work on, (1944) 61
 salmonellas causing, (1944) 235
 requirements and intakes, (1943) 214; (1944) 235
 simple dietaries, (1941-2) 232
 war-time, in, (1943) 214-6
 winter, in, (1943) 216
- Foot
 assessment of function, (1943) 217
 contact dermatitis, (1944) 198
 defects in children, (1944) 236
 dermatitis, (1944) 198
 dermatophytosis, (1941-2) 233
 diseases, (1940) 302; (1941-2) 232; (1944) 236
 deformities, and, (1939) 342; (1940) 302, (1941-1942) 232; (1944) 236
 military service, and, (1941-2) 232
 flat, (1939) 342 *See also* Flat-foot
 fracture,
 bilateral march, (1941-2) 211
 or callos, of, (1944) 206
 gangrene of, complicating scarlet fever, (1941-2) 378
 immersion, (1944) 239
 pain, in acromegaly, (1941-2) 129
 painful, (1944) 236-9
 soldiers, in, (1944) 236

CUMULATIVE INDEX

Foot—*continued*

- painful conditions of, (1943) 217. *See also* Chilblains
- foot-roller treatment for, (1939) 342
- ringworm, (1941-2) 233
- 'shelter', (1943) 2
- strain in war-workers, (1944) 236
- super-numerary metatarsal bone, (1941-2) 232
- trench, (1940) 303; (1943) 1
- trophic disturbances, (1940) 303
- tumours, primary, of, (1940) 302
- Forces. *See also* Aviators; Soldiers; Injuries, Effort syndrome, War
- digestive diseases in, (1944) 214
- dyspepsia, gastroscopic findings in, (1944) 222
- group intelligence tests in, (1944) 78
- impetigo in, (1944) 257
- malingerer in, (1944) 79, 297
- night-blindness in, (1944) 158
- peptic ulcer in, treatment for, (1944) 319
- psychoneuroses in, (1944) 340-5
- psychoses in, (1944) 79
- sciatica in, (1944) 364
- varicose veins in, (1944) 400
- venereal diseases in, (1944) 102
- Foreign bodies
- arthritis, causing, (1940) 360
- bladder, in, (1941-2) 161
- eye, in, (1943) 79
- heart and pericardium, in, (1940) 333, (1941-2) 249
- intestinal perforation ducts, (1944) 120
- localization by X-rays, (1944) 355
- military surgery, in, (1944) 18
- stomach, in, (1940) 546, (1943) 353
- X-ray examination, (1941-2) 371
- Formic acid in pulmonary tuberculosis, (1943) 414
- Formol-gel reaction, (1939) 246
- diagnosis of rheumatic diseases, in, (1941-2) 154
- Fornix, posterior, needle puncture of, (1940) 23
- Fouadin
- abortion fever, in, (1939) 183
- stibophen, official name for, (1940) 127
- ulcerative granuloma treated by sulphapyridine and, (1941-2) 239
- Fox-Fordyce disease, (1944) 374
- Fracture, (1941-2) 210, (1943) 193
- anaesthesia, (1940) 177, 276
- ankle joint, osteoarthritis complicating, (1941-2) 211
- carpal cuneiform bone, (1943) 194
- carpal scaphoid, internal fixation of, (1941-2) 211
- clay-shoveller's, (1940) 276
- compound,
 - chemotherapy, (1944) 206
 - closed plaster method, treatment by, (1941-2) 267
 - treatment of, (1943) 194
- convulsion therapy,
 - causing, (1940) 491, (1941-2) 366
 - complicating, (1940) 59
- delayed union, (1940) 273, (1943) 193, (1944) 205
- early function, (1943) 196
- fat embolism complicating, (1940) 274
- fatigue, of tibia, (1944) 206
- femur, of, (1941-2) 14, (1943) 195
- non-union, treatment of, (1940) 274
- foot, (1941-2) 211, (1944) 206
- forearm, (1943) 194
- immobilization, (1943) 195
- internal fixation in conjunction with sulphanilamide, (1941-2) 210
- knee, new method of approach, (1940) 275
- leptazol shock therapy causing, (1941-2) 366
- march, bilateral, (1941-2) 211
- minor, local anaesthesia in treatment, (1940) 276
- non-union, treatment, (1940) 273
- olecranon, of, (1941-2) 14
- os calcis, treated by triple arthrodesis, (1944) 206
- pathological, multiple, in Pott's disease, (1940) 536
- pseudo-, (1941-2) 171
- radius and ulna, shafts of, (1943) 194
- recurrent, (1943) 193
- rehabilitation, (1943) 196
- replacement, exact, (1943) 195

Fracture—*continued*

- restoration of function after, (1943) 195
- skull, and injury to posterior pituitary, (1941-2) 174
- soldiers, in, (1943) 12
- spine, clay-shoveller's fracture, (1940) 276
- splintage, use of vitalium, (1941-2) 210
- tibia, (1943) 193
- 'birth-fracture' of, (1940) 275
- fatigue fracture of, (1944) 206
- pseudo-fracture of, (1940) 275
- treatment,
 - internal fixation in conjunction with sulphanilamide, (1941-2) 210
 - surgical, (1939) 27
 - vitalium appliances, (1941-2) 210
- ulna, (1943) 194
- dislocation of head of radius associated with, (1940) 276
- union, (1940) 273
- oestrogens, effect of, (1940) 273; (1941-2) 211
- testosterone, effect of, (1940) 273
- vitamin E, effect of, (1940) 273
- wrist joint, of, (1941-2) 211
- Fragarine, relief of dysmenorrhoea and labour pains by, (1943) 96
- Fragilitas ossium, idiopathic, (1941-2) 171, (1943) 159
- Frei antigens, lymphopathia venereum, in, (1940) 92
- Frei test, (1941-2) 109
- lymphopathia venereum, in, (1943) 92
- Freud, influence of, (1940) 7
- Friedman test, (1940) 246, 478
- ovarian pregnancy, in, (1940) 481
- positive results in non-pregnant states, (1941-2) 358
- quantitative, (1940) 246
- Froehlich's syndrome, pituitary function in, (1940) 152
- Frontal
- leucotomy,
 - mental disorders, treatment of, in, (1941-2) 81, (1943) 67
 - technique, (1941-2) 82
- lobe,
 - lesions of, (1940) 228
 - mental changes resulting from, (1940) 71-3
 - symptom-complexes associated with, (1941-2) 174
- lobectomy, (1940) 225, 228
- sinus, absence or imperfect development of, (1943) 103
- Frost-bite, (1940) 303; (1943) 1, (1944) 239
- aviators, in, (1941-2) 35
- treatment, (1943) 217
- Fructose (laevulose) tolerance test, liver function, of, (1940) 116
- Fruit juice, effect on gastric function, (1941-2) 259
- Fundus oculi
 - atropine, dangers of, (1944) 232
 - reflexes of, importance of, (1941-2) 227
- Fungi, pruritus ani caused by, (1939) 221
- Fungicidal dusts, poisoning from inhalation of, (1941-2) 411
- Fungous diseases, (1939) 342; (1940) 304; (1941-2) 217, 233
- feet and hands, of, (1939) 343
- gentian violet and brilliant green in, (1940) 304
- scalp, kerion of, (1939) 342
- skin, of, (1939) 64
- skin allergy due to, (1941-2) 137
- surfer's feet, bacteriology and treatment of, (1939) 343
- sweat components, fungicidal properties of, (1939) 343
- treatment, (1940) 304
- vaccines, (1939) 343
- vagina and vulva during pregnancy, (1940) 594
- Fungal infection, brain, of, (1941-2) 173
- Fuifuryl trimethyl ammonium iodide, intravenous drip administration, (1941-2) 346
- Fur industry, diseases, (1944) 260
- Furunculosis. *See* Boils

CUMULATIVE INDEX

G

- Galactorrhoea, treatment of, (1939) 220
- Galactose tolerance test, (1940) 316, 385, (1943) 267
- Galactosuria, jaundice, in, (1940) 359
- Gall-bladder, (1941-2) 233
 - absence, congenital, carcinoma of common duct associated with, (1940) 305
 - adhesions of cholecysto-hepatic flexure, (1940) 307
 - calcium carbonate deposits in, (1940) 306
 - cholesterosis of, (1941-2) 233
 - congenital abnormalities, (1940) 305
 - constipation and, (1944) 189
 - diseases, (1940) 305-8
 - diverticulosis of, (1943) 218
 - double, (1940) 305, (1943) 219
 - function of, (1943) 219
 - disturbance of, (1941-2) 233
 - giardial infection, (1941-2) 24
 - physiology, (1941-2) 233
 - roentgenography, (1941-2) 234
 - strawberry, (1941-2) 233
 - surgery of, (1940) 13
 - tuberculosis, of, (1940) 305
 - X-ray examination, (1940) 503
- Gall-bladder and bile-ducts, (1939) 344
- cholangitis, (1939) 347
 - micro-organisms found in, (1939) 49
- cholecystitis, (1939) 346
- gall-bladder surgery, (1939) 27
- gall-stones, (1939) 344
 - composition, (1939) 344
 - diagnosis of, (1939) 49, 344
 - ether injection treatment, (1939) 345
 - faeces, in, (1939) 344
 - intestinal obstruction caused by, (1939) 344
 - urinary diastase, (1939) 345
- Gallp rhythm, systolic, mechanism of, (1940) 192
- Gall-stones, (1941-2) 233
 - bile-duct, left-sided pain in, (1943) 219
 - calcium bilirubinate pigment and cholesterol in faeces, (1940) 306
 - calcium carbonate, (1940) 306
 - carcinoma of intrahepatic bile-ducts and, (1944) 290
 - clinical picture, (1940) 306
 - diagnosis, (1940) 306
 - ileus, recurrent, (1941-2) 125
 - intestinal obstruction due to, (1941-2) 125
- Ganglion
 - injection treatment, (1941-2) 243
 - X-ray treatment, (1941-2) 243
- Ganglioneuroma, mediastinum, of, (1941-2) 303
- Gangrene
 - antitoxin, in treatment of cancerum oris, (1940) 242
 - diabetes mellitus, in, (1940) 263
 - feet, of, complicating fever, (1941-2) 378
 - gas *See also* Gas gangrene
 - sulphanilamides in, (1941-2) 341
 - lung, of, (1939) 410
 - skin, of, progressive, (1941-2) 392
- Gangrenous balanitis, hydrogen peroxide in, (1939) 155
- Gargoylism, (1943) 220
- Garlock's operation for removal of thoracic oesophagus, (1940) 13
- Gas
 - attack, precautions against, (1944) 8
 - cysts, intestine, of, (1941-2) 272
 - poisoning, (1941-2) 408
- Gas gangrene
 - aetiology, (1940) 308
 - diagnosis, (1940) 308
 - G. perfringens* cause of, (1940) 308
 - injections, introduction of spores by, (1940) 308
 - knowledge of, gained in war, (1940) 3
 - prophylaxis of, (1939) 385
 - radiography in, (1940) 308
 - treatment, (1940) 309
 - cauterization, extensive, (1940) 310
 - serum, (1940) 309
 - sulphanilamides, (1941-2) 341
 - sulphonamides, (1940) 309
 - X-ray, (1944) 241

Gases

- irritant, in industry, (1944) 386
- poisonous,
 - industry, in, (1940) 310
 - ocular lesions, (1943) 80
 - warfare, in, (1943) 220. *See also* Mustard-gas
- asphyxiant, (1940) 310
- lung-irritant, (1940) 310
- mustard-gas, (1940) 311
- phosgene, (1940) 310
- vesicant, (1940) 311
- Gasoline, poisoning by, (1943) 363
- Gasserian ganglion
 - injection of, in trigeminal neuralgia, (1940) 423
 - tumours of, (1944) 165
- Gastrectomy, (1941-2) 14
 - Billroth I method, (1940) 13
 - partial, for peptic ulcer, (1941-2) 326
 - Polya's method, (1940) 13
 - total, for carcinoma of stomach, (1940) 545
 - partial oesophagectomy, and, (1941-2) 401
 - technique, (1941-2) 401
- Gastric
 - acidity,
 - antacids, effects of, (1940) 439
 - blood CO₂ and dehydration, relation to, (1940) 437
 - control by diet and drugs, (1943) 245
 - gastric resection and, (1941-2) 327
 - nicotine, effect of, (1941-2) 326
 - peptic ulcer, in, (1940) 437
 - changes following injury to posterior pituitary, (1941-2) 174
 - crises, chordotomy, anterior, for, (1940) 426
 - disorders, (1939) 21
 - dental deficiency and, (1944) 31
 - soldiers, in, (1940) 25
 - teeth and, (1944) 31
 - function, effect of fruit juice on, (1941-2) 259
 - lavage, pulmonary tuberculosis, in, (1941-2) 292
 - tuberculosis, in, (1940) 389
 - mucosa,
 - effect of alcohol on, (1941-2) 135
 - presence of spirochaetes in, (1941-2) 401
 - neurilemmoma, (1943) 353
 - neurosis, (1944) 30
 - polyp, (1944) 380
 - polypsis, (1943) 352
 - secretion,
 - barbiturates, effect of, (1940) 557
 - carcinoma extracts, depressant effect of, on, (1941-2) 401
 - megaloeytic anaemia of pregnancy, and, (1940) 171
 - treatment, vitamin A (avoelium), (1941-2) 327
 - ulcer *See also* Peptic ulcer
- alkali poisoning in, (1941-2) 135
- carcinoma, differential diagnosis from, (1940) 545
 - haemorrhage complicating, (1943) 45
 - incidence relative to duodenal ulcer, (1944) 31
 - presence of spirochaetes in gastric mucosa, (1941-2) 401
 - soldiers, in, (1940) 25
 - treatment, surgical, (1940) 442
- Gastric and duodenal ulcer
 - aetiology and treatment of, unsolved problems in, (1940) 5
 - alkaline drugs in, (1940) 5
 - feeding in cases of, (1940) 5
 - perforation of, (1940) 12
 - partial gastrectomy in, (1940) 12
 - treatment of, (1939) 46
- Gastritis, (1943) 221
 - alcoholism causing, (1941-2) 135, (1943) 46
 - carcinoma, differential diagnosis from, (1940) 311
 - chronic,
 - atrophic, desiccated hog's-stomach in, (1940) 312
 - follicular, (1943) 222
 - diagnosis, and differential diagnosis of, (1939) 47, (1940) 311
 - hypertrophic, (1944) 30
 - morbid anatomy, (1944) 242
 - pathology, (1944) 242

CUMULATIVE INDEX

Gastritis—continued

- polypoid, (1944) 380
- radiology and gastroscopy in, (1943) 221
- syphilis in relation to, (1941-2) 234
- treatment, (1940) 312
- tuberculosis, experimental, (1944) 242
- Gastro-colic fistula, (1941-2) 329
- Gastro-duodenal haemorrhage
 - diagnosis, (1943) 45
 - treatment, (1943) 45
- Gastro-enteritis
 - acidosis, associated with, (1941-2) 128
 - blood changes in, (1941-2) 128
- Gastro-enterostomy
 - congenital duodenal obstruction, in, (1943) 253
 - megaloeytic anaemia after, (1943) 116
- Gastro-intestinal allergy
 - children, in, (1940) 163
 - milk as cause of, (1941-2) 138
- disease
 - incidence during the war, (1941-2) 215
 - nicotinic acid deficiency cause of, (1939) 14
 - phenolphthalein test in, (1940) 544
 - present state of knowledge of, (1940) 5
 - trientin as antispasmodic in, (1940) 462
 - vitamin B deficiency causing, (1943) 189
- disorders, (1943) 45
- haemorrhage, transfusion of whole blood in, (1941-2) 169
- symptoms
 - old age, in, (1941-2) 380
 - osteoporosis in, (1940) 225
 - pulmonary tuberculosis, in, (1941-2) 292
- tract
 - leiomyoma of, (1943) 370
 - lymphoid tumours primary solitary, (1943) 274
 - ulceration, phenolphthalein test in, (1941-2) 273
- Gastro-jejunal ulcer, (1941-2) 328
 - clinical picture and morbid anatomy, (1941-2) 328
 - gastro-colic and gastro-jejuno-colic fistula complicating, (1941-2) 329
- Gastro-jejuno-colic fistula, (1941-2) 329
- Gastro-jejunostomy, gastroscopy in complications following, (1939) 48
- Gastroscope
 - diagnosis, value in, (1939) 21
 - Schindler's flexible, (1939) 47
- Gastroscopy, (1939) 47, (1941-2) 3
 - comparative values of radiology and, (1943) 202
 - dyspepsia, in, (1944) 222
 - gastritis, in, (1943) 221
 - hypertrophic, in, (1944) 30
 - pernicious anaemia, in, (1939) 203
- Gaucher's disease
 - biopsy examination of pingueculae, (1941-2) 287
 - diagnosis by sternal puncture, (1941-2) 287
 - lipid analysis of spleen, (1943) 265
 - treatment, bistoval as adjuvant in malarial therapy, (1943) 292
- Gelatin, effect on muscular fatigue, (1941-2) 331
 - solutions, transfusion of, (1944) 162
- General medicine, (1939) 12
 - cause of disease, (1939) 12
 - prevention and treatment, (1939) 16
 - symptoms, mechanism and treatment of, (1939) 19
- General paralysis, brain tumour diagnosis from, (1939) 260
- General paralysis of the insane, (1941-2) 315
 - aetiology and treatment of, (1939) 447
 - incidence and aetiological factors, (1943) 292
 - 'stationary', (1940) 425
 - treatment, (1940) 60, 425, (1941-2) 315
 - artificial fever and malaria therapy compared, (1941-2) 315
 - combined artificial fever, chemotherapy, and vaccino-therapy, (1941-2) 315
 - pyretotherapy, (1941-2) 105
 - R. tsutsugamushi*, injection of, (1940) 425
- Geniculate body, lateral, (1943) 73
- Genital, cancer, subarachnoid injections of alcohol in, (1941-2) 185

Genitalia

- infantilism, hormone treatment, (1943) 197
- ulcers, recurrent, in mouth and, (1943) 20
- Genito-urinary diseases, (1940) 14
 - operations, (1939) 27
 - surgery, advances in, (1940) 14
 - symptoms, associated with allergy, (1940) 164
 - tract, *Trichomonas vaginalis* infestation in male, (1941-2) 417
- Gentian violet
 - blepharitis treated with, (1941-2) 227
 - burns treated with, (1941-2) 181
 - dermatitis caused by, (1941-2) 203
 - oxyuriasis treated with, (1940) 419, (1943) 287, (1944) 309
 - tinia capitis treated with, (1940) 304
- German measles, rheumatic manifestations, (1940) 312
- Germanin, suramin, official name for, (1940) 127
- Giant-celled tumour
 - bone, of, (1941-2) 172
 - subperiosteal, of mandible, (1940) 228
- Giant cells, prodromal stage of measles, in, (1940) 401
- Giardia intestinalis*, (1941-2) 24
 - infestation with, (1940) 269
 - diarrhoea associated with, (1941-2) 208
 - enteritis associated with, (1944) 202
 - steatorrhoea associated with, (1944) 203
 - treatment of, (1939) 310
- Giardiasis, (1941-2) 24
 - clinical picture, (1941-2) 24
 - diarrhoea associated with, (1941-2) 208
 - treatment, (1941-2) 24
- Gierke's disease, (1940) 314
- Gigantism, hyperpituitary, (1940) 467
- Gingivitis
 - ascorbic acid in treatment, (1941-2) 308
 - chromium trioxide, treatment with, (1941-2) 307
 - short-wave therapy in, (1941-2) 202
- Glandular fever, (1939) 348, (1941-2) 235
 - aetiology, (1941-2) 235
 - agglutination reaction, (1940) 313
 - tests, (1941-2) 235
 - angina of throat associated with, (1941-2) 235
 - blood picture, atypical, (1941-2) 235
 - clinical picture, (1940) 312, (1941-2) 235
 - diagnosis, and, (1939) 348
 - complications, (1941-2) 235
 - diagnosis and differential diagnosis, (1940) 313, (1941-2) 235
 - Paul-Bunnell test (1941-2) 235, (1943) 222
 - Pfeiffer's bacillus infection, (1943) 223
 - exanthem, (1940) 312
 - jaundice complicating, (1943) 222
 - positive syphilitic reactions in, (1943) 88
 - serological test for, (1939) 53
 - simulating diphtheria, (1941-2) 235
 - splenic rupture in, (1941-2) 235
 - treatment, (1940) 313
 - sulphapyridine in, (1940) 313, (1941-2) 118
- Glare
 - affecting eyes of aviators, (1941-2) 36
 - colour, and, (1944) 259
- Glass, eye injuries from broken, (1940) 253
- Glaucoma, (1939) 349
 - aetiology, (1939) 349, (1940) 313
 - anxiety states as aetiological factor, (1940) 313
 - mecholyt, (1939) 350
 - prostigmin, (1939) 350
 - radiotherapy, (1940) 313
 - sorbitol, (1939) 350
 - spleen extract treatment, (1939) 351
 - survey of, (1939) 129
 - treatment
 - surgical, and results of, (1939) 350, (1944) 242
- Glioma
 - cerebellum, in
 - classification and symptoms of, (1939) 97
 - corpora quadrigemina and pineal body, (1939) 98
 - frontal lobe, (1939) 99

CUMULATIVE INDEX

- Glioma**—*continued*
cerebellum, in—*continued*
pons and medulla, (1939) 96
temporal lobe, (1939) 98
cerebral, lobectomy in treatment of, (1940) 73
retina, of, (1943) 326
Globin (zinc) insulin, (1943) 34
Globulin serum, in prophylaxis of measles, (1943) 279
Globulins, plasma, in, (1940) 121
Globus pallidus, functions of, (1941–2) 90
Glomangioma, (1940) 533
Glomerulo-nephritis, (1941–2) 312
acute,
children, in, (1941–2) 313
hypertension and, (1941–2) 312
treatment by magnesium sulphate, (1941–2) 312
children, in, (1941–2) 313
chronic,
calcium plaques in, (1941–2) 312
diffuse, vascular phase of, (1944) 311
clinical
course and diagnosis, (1943) 288
course and prognosis, (1941–2) 313
picture, (1941–2) 313
histological changes, (1944) 310
magnesium sulphate treatment of convulsions, (1943) 289
morbid anatomy, (1944) 310
pregnancy, in, (1940) 17
prophylaxis by tonsillectomy, (1944) 309
treatment, ascorbic acid in, (1940) 422
Glomerulosclerosis
intercapillary, (1940) 421
diabetes mellitus, and, (1941–2) 152, (1943) 288
Glomus tumour, (1941–2) 393
diagnosis, (1943) 346
histology, (1943) 345
morbid anatomy, (1943) 345
nail, of, (1941–2) 311
synovial membrane of knee, on, (1941–2) 393
Glossitis, (1939) 434
nicotinic acid deficiency cause of, (1939) 14
vitamin deficiency in, (1941–2) 424
Gloves, surgical, shortage of, (1944) 14
Glucuronic acid excretion test, liver function of, (1940) 117
Glucose
addition to stored blood, (1943) 155
alcoholism, in, insulin and, (1940) 157
brain metabolism, in, (1940) 119
cardiac disease, hypertonic injections in, (1941–2) 340
haematemesis, in, treatment of, (1943) 228
ingestion, and plasma potassium, (1940) 113
metabolism, role of vitamin B₁ in, (1940) 114
tolerance,
staphylococcal infection, and, (1941–2) 306
test,
diabetes mellitus, in, (1940) 263
intravenous, (1940) 264
one-hour two-dose, (1940) 263
war wounds, surgical treatment of, in (1943) 248
Glutamic acid, effect on lactation, (1941–2) 262
Gluteus medius muscle, defect of, postural treatment, (1941–2) 310
Glycerin injections in gonorrhoea, (1939) 356
Glycerin-sulphonamide paste, burns treated with, (1941–2) 182
Glycerin-syrup substitute, (1943) 94
Glyceryl trinitrate (nitroglycerine) in colic, (1939) 165
Glycine, effect on actation, (1941–2) 262
Glycogen
disease, (1939) 351; (1940) 314
actiology, (1940) 314
metabolism, vitamin B complex and, (1944) 243
Glycosuria, actiology and diagnosis, (1939) 352
Goeckerman treatment for psoriasis, (1944) 338
Goitre and other diseases of thyroid gland, (1939) 353; (1940) 314–7; (1941–2) 235
adenomas, (1939) 355
calcium and phosphorus metabolism in, (1943) 223
Goitre—*continued*
congenital, (1940) 315
sporadic, (1940) 315
endemic, fluorine and, (1941–2) 235
iodine and, (1940) 314
simple, geological distribution of fluorine in relation to, (1941–2) 235
thyroiditis, Riedel's, radium therapy in, (1939) 355
toxic, (1939) 352, (1941–2) 236; (1943) 223; (1944) 46
anaesthetics in operation for, (1939) 210
calcium and phosphorus metabolism, (1941–2) 236
children, in, (1939) 354
clinical picture, (1941–2) 236
diagnosis of masked hyperthyroidism, (1943) 224
diarrhoea, acetylcholine in, (1939) 354
excretion of hippuric acid in, (1941–2) 236
exophthalmos in, (1940) 316
cause of, (1939) 352
hippuric acid test, (1940) 317
presence of sympathetic paralysis, in, (1940) 316
iodine content of blood and urine, (1939) 353
masked symptoms, (1939) 353
myasthenia gravis associated with, (1943) 224
hyperplastic thymus associated with, and, (1939) 353
neck movements, effect of, (1939) 352
oedema and jaundice, hepatitis as cause of, (1939) 353
pathology, (1941–2) 236, (1944) 243
plump type, (1943) 223
treatment, ergot alkaloids, ergotoxine and ergotamine, (1941–2) 236
vitamin B complex and glycogen metabolism, (1944) 243
vitamin C therapy, (1939) 354
Gold
compounds,
agranulocytosis caused by, (1940) 156
arthritis treated with, (1940) 200
lupus erythematosus treated with, (1943) 273
rheumatoid arthritis treated with, (1940) 198, (1941–2) 154; (1944) 137, (1944) 153
therapy,
arthritis, in, (1939) 229
myocrisin in osteoarthritis, (1939) 228
parmanil in rheumatoid arthritis, (1939) 226
vulvovagino-cervicitis due to, (1944) 405
Gonad extracts, malignant disease treated with, (1941–2) 184
Gonadotrophic hormone *See* Hormone therapy; Hormones
ovary, effect on, (1943) 20
undescended testis treated with, (1941–2) 406
chorionic, (1941–2) 406
Gonadotrophic stimulation, climacteric, relation to, (1939) 279
Gonadotropius, pituitary, synergism of oestrogens with, (1941–2) 384
Gonococcal
arthritis,
clinical picture, (1944) 151
incidence, (1944) 151
keratosis blennorrhagica, and, (1943) 136
sulphanilamide treatment, (1940) 197
sulphonamide treatment, (1940) 91
conjunctivitis, (1943) 178
myocarditis, (1940) 333
ophthalmia, sulphanilamide in, (1940) 251
septicaemia,
associated with endocarditis, (1941–2) 237
treatment, (1941–2) 238
vaginitis in children, (1943) 91, 226
oestrogenic therapy, (1940) 594
vulvovaginitis, (1940) 319
Gonococcus
cultivation of, (1943) 90
M & B 693, effect of, on, (1940) 134
sulphanilamide, action on, (1940) 133
Gonorrhoea, (1939) 356; (1941–2) 107, 237; (1943) 21, 90, 226

CUMULATIVE INDEX

Gonorrhoea—continued

- adult female, in, (1939) 356
 - ergotamine tartrate in diagnosis, (1939) 356
 - sulphonamides, (1939) 357; (1944) 28
 - tests of cure, (1939) 357
- albucid in, (1939) 171, 357; (1940) 319
- bacteriological tests, (1943) 21, 90
- bacteriology, (1941-2) 237
- both sexes, in, (1939) 357
 - carriers, (1939) 358
 - diagnosis, (1939) 357
 - fever therapy, (1939) 358
 - liver damage, (1939) 357
 - sulphonamides, (1939) 155, 358
- children, in,
 - vulvovaginitis, (1939) 359
 - fever therapy, (1939) 359
 - oestrogens, (1939) 359
 - sulphanilamide, (1939) 359
 - theelin, (1939) 359
- cultural diagnosis, (1944) 106
- diagnosis, (1940) 90; (1941-2) 107
- diagnostic cutaneous test, (1941-2) 237
- M & B 693 in, (1939) 155, 171, 356
- male, in, (1939) 356, (1940) 318
 - glycerin injections, (1939) 356
 - M & B 693 and mercuric irrigations, (1939) 356
 - prophylaxis, (1944) 244
 - treatment, (1941-2) 237, (1943) 243
 - albucid, (1941-2) 237
 - sulphapyridine, (1941-2) 237
 - sulphathiazole, (1941-2) 237
 - sulphamethylthiazole, and, (1941-2) 238
 - sulphapyridine, and, (1941-2) 238
 - toxic effects of, (1941-2) 238
- pathology, (1941-2) 237
- salpingitis, oestrogenic therapy, (1941-2) 228
- sulphonamides in, (1939) 17, 171
 - prevention and treatment, in, (1944) 107
 - prophylaxis by, (1944) 107
 - possible ill effects, (1944) 107
 - resistance in, (1944) 108, 112
- survey of, (1939) 155
- tests of cure, (1943) 90
- treatment,
 - albucid, (1940) 319
 - artificial fever and chemotherapy, (1941-2) 238, (1944) 243
 - artificial hyperpyrexia and sulphanilamide, (1940) 319
- females, in,
 - sulphanilamide, (1943) 21
 - sulphathiazole, (1943) 226
- males, in,
 - sulphapyridine, (1943) 91
 - sulphathiazole, (1943) 91
 - penicillin, (1944) 108
 - sulphanilamide, (1940) 319
 - sulphapyridine, (1940) 90, 318; (1941-2) 117
 - mercuric oxycyanide irrigations, and, (1940) 318
 - sulphathiazole, (1941-2) 107
 - sulphonamides, (1940) 90, (1941-2) 107, (1944) 107
 - causes of failure, (1944) 107
 - pyrexial treatment, with, (1941-2) 108
 - ulcer in, (1939) 170, 357
- Gonorrhoeal ophthalmia, (1943) 178
- epidemic, in children, (1943) 178
- Goormaghtigh cells, (1944) 161
- Gordon's reaction, Hodgkin's disease, in, (1941-2) 258
- Gout, (1939) 359; (1940) 321
 - aetiology, (1940) 321
 - diagnosis and differential diagnosis of, (1941-2) 239
 - diet, (1939) 360
 - early life, in, (1940) 322
 - hermaphroditism associated with, (1943) 226
 - high fat diet as cause of, (1940) 321
 - rheumatism, relation to, (1940) 321
 - salysrgan, after, (1939) 359
 - treatment, (1943) 227
 - dietetic, (1944) 244
 - low fat high carbohydrate diet, (1944) 244
 - vitamin B₁, (1944) 244

- Grafting, skin, (1941-2) 264
- Gramicidin, (1944) 116
 - bactericidal effects of, (1943) 308
- Gram's stain, discovery of, (1940) 7
- Granuloma
 - annular, resemblance to necrobiosis lipidica, (1943) 347
 - cervix, of, (1940) 322
 - coccidioidal, (1943) 145
 - inguinale, (1940) 91; (1941-2) 109
 - magnesium silicate, (1944) 208
 - pyogenicum, X-ray therapy, (1940) 532
 - stibophen in, (1940) 136
 - traumatic, of synovial membrane, (1941-2) 274
 - ulcerative, (1940) 91, (1943) 227
 - treatment,
 - radiotherapy in, (1939) 514
 - sulphapyridine with foudain, (1941-2) 239
 - venereum, antimony in, (1939) 155
 - vulva, of, infective, (1940) 593
- Granulomatosis
 - cholesterol, acute idiopathic, (1943) 266
 - lipoid *See* Schuller-Christian syndrome
 - lipophagic, of enteric tract, (1943) 266
- Granulosa-celled and theca-celled tumours of ovary, (1941-2) 320
- Granulosa-celled tumours of ovary, (1940) 428
- Grasset's tubercle endotoxoid
 - leprosy treated with, (1941-2) 284
 - lupus vulgaris treated with, (1941-2) 300
- Graves's disease *See* Goitre, toxic
- Grenz ray
 - port-wine birthmarks treated with, (1940) 187
 - skin diseases, treatment in, (1943) 323
- Group
 - intelligence tests, (1944) 78
 - psychotherapy, (1944) 74
- 'Growing pains', rheumatism, relation to, (1939) 136
- Growth
 - pituitary and thyroid, effects of, (1940) 281
 - vitamin A and, (1940) 128
- Growth hormone, (1941-2) 351
 - (antutrin-growth), (1939) 108
- Guandine, myasthenia gravis treated with, (1940) 417, (1943) 285
- Guandine hydrochloride, myasthenia gravis treated with, (1940) 417
- Guillain-Barre syndrome, (1941-2) 315; (1943) 291
 - cerebellar form of, (1939) 273
- Guillotine amputation, (1940) 11
- Guinea-worm
 - geographical distribution, (1944) 244
 - treatment by injections of phenothiazine, (1943) 228
- Gum
 - acacia, as cause of asthma, (1941-2) 157
 - karaya, allergic reaction to, (1940) 150
- Gums
 - benign hyperplasia of, in epileptics, (1941-2) 222
 - hypertrophy of, (1941-2) 230
- Gynaecology, advances in, (1940) 20-4, (1941-2) 16, (1943) 19, (1944) 25
 - sulphanilamide powder in, (1944) 25
 - survey of, (1939) 33
- Gynaecomastia
 - men, in, (1944) 19
 - stilboestrol as cause of, (1941-2) 383
 - symptom of extra-genital chorion-epithelioma, (1941-2) 190
- Gynandroblastoma, (1944) 314

H

- Habit formation, influence of faulty, (1944) 75
- Haemangioma
 - scrotum, of, (1941-2) 325
 - uterus, of, (1941-2) 419
- Haemaphysalis leachi*, vector of tick-bite fever, (1940) 81
- Haematemesis, (1939) 360
 - aetiology, (1940) 322
 - aspirin as cause of, (1939) 48
 - ingestion of, causing, (1940) 322
 - blindness after, (1941-2) 162
 - drop blood transfusion in, (1939) 360

CUMULATIVE INDEX

Haematemesis - continued

- emotional stress in aetiology of, (1939) 360
- feeding in cases of, (1940) 5
- gastroscopy in, (1939) 48
- probable advances in treatment of, (1939) 21
- prognosis, (1939) 360
- treatment of, (1939) 47
 - grave cases, (1943) 45, 228
 - Meulengracht regimen, (1943) 300

Haematocolpos, imperforate hymen, with, (1940) 592

Haematology

- advances in, (1941-2) 6
- survey of, (1939) 21, 52

Haematoma

- post-partum labial and paravaginal, (1940) 593
- rectus abdominis muscle, of, (1943) 282
- sarcoma arising from, (1941-2) 183

Haematoporphyrin

- biochemistry of, (1940) 119
- blood sugar, action on, (1939) 306
- depression treated with, (1940) 487
- pyramidal hypertonia, (1940) 415
- Haematoporphyrinuria, (1940) 323, (1944) 245
 - acute, (1943) 228
 - complicated by acute polyneuritis, (1941-2) 239
 - aetiology of, (1939) 361
 - biochemical, (1940) 323
 - clinical picture, (1940) 323

Haematuria

- aetiology, (1944) 245
- essential, renal papilla causing, (1943) 229
- hypernephroma causing, (1941-2) 277
- occult, (1940) 575
- sulphadiazine causing, (1943) 245
- sulphapyridine causing, (1940) 324, 367
- sulphathiazole causing, (1940) 367, (1941-2) 240
- sulphonamides causing, (1939) 177, (1941-2) 116, 346
- vitamin C therapy in, (1939) 361

Haemochromatosis, (1943) 118

- anomalous symptoms in, (1941-2) 240

Haemoglobin, (1941-2) 7

- diet and, (1944) 131
- extra-corporeal circulating, fate of, (1941-2) 170
- haemorrhage, effects of, (1943) 147
- injections of, (1941-2) 170
- metabolism, (1940) 119, 458, (1943) 25
 - effect of sulphonamides on, (1940) 458
- puerperal morbidity and, (1944) 23
- solution as blood substitute, (1940) 218
- women and children, in, (1944) 158

Haemoglobinaemia, (1941-2) 170

- paroxysmal nocturnal, (1941-2) 140

Haemoglobinuria

- chronic haemolytic anaemia with, (1941-2) 140
- exercise, (1943) 4
- march, (1943) 4
- paroxysmal, (1944) 245
- sulphanilamide causing, (1941-2) 240

Haemoglobinuric fever, (1943) 144 See Blackwater fever

Haemolysis

- blood, preserved, in, (1940) 220
- factors influencing, (1940) 220
- intravascular, (1941-2) 7

- blood transfusion, after, (1943) 156

Haemolytic anaemia See Anaemia, haemolytic

Haemophilia, (1939) 361

- aetiology, (1939) 361, (1940) 325
- coagulation of blood plasma, (1940) 325
- heparin, effects of, (1944) 159
- incidence, (1940) 325
- ovarian extract, (1939) 362
- problems, unsolved, in, (1940) 6
- pseudo-, with gastric haemorrhage, (1943) 229
- sex ratios in families, (1940) 325
- thrombin, delayed formation of, (1940) 325
- treatment, (1939) 362, (1944) 246
 - dried human plasma, with, (1943) 229

Haemophilus

influenzae,

- adrenal haemorrhage caused by, (1941-2) 132
- meningitis caused by, (1940) 404; (1941-2) 305
- para-influenzae, endocarditis due to, (1940) 334

Haemophilus—continued

pertussis,

- nasopharyngeal cultures and cough-plate cultures, (1944) 407
- variant phases of, (1944) 406

Haempneumothorax, treatment of, (1943) 311

Haemopoietin, (1943) 47

Haemoptysis

- Hodgkin's disease, in, (1941-2) 258
- oxygen injection in, (1939) 362
- prothrombin deficiency in, (1943) 230
- pulmonary tuberculosis in, (1939) 411
- vitamin K in, (1943) 63, 230

Haemorrhage

adrenal,

- acute bilateral, (1941-2) 132
- meningococcal septicaemia associated with, (1941-2) 186

- pregnancy, in, (1941-2) 358

- allergy induced by anti-haemorrhagic substances, (1941-2) 170

- arterial, control of, (1940) 347

- aural, caused by aneurysm of internal carotid, (1941-2) 144

- blindness after, (1941-2) 162

- blood cells, effects on, (1943) 147

- blood substitutes in, (1940) 6, 218

- blood transfusion in, (1940) 222

- diabetes mellitus, in, (1943) 186

- familial haemorrhagic telangiectasia, associated with, (1941-2) 223

- gastric, uraemia after, (1943) 372

- gastro-duodenal, (1940) 438, (1943) 45, 228

- gastro-intestinal, blood chemistry in, (1941-2) 139

- transfusion of whole blood in, (1941-2) 169

- hypoprothrombinaemic, after operation for appendicitis, (1941-2) 149

- intracranial, new-born, in, (1940) 32

- intravenous injections of sodium ascorbate, (1941-2) 269

- islinglass, transfusions of, (1941-2) 269

- neonatal, (1940) 16

- blood transfusion in, (1939) 250

- vitamin K,

- antenatal administration of, (1944) 246

- therapy, (1941-2) 427

- pernicious, in peptic ulcer, (1940) 438

- petechial, anti-syphilitic therapy causing, (1941-2) 405

- post-operative, vitamin K and cholic acid in, (1940) 357

- prothrombin and vitamin K in relation to, (1940) 117

- rabbit thrombin in, (1943) 118

- rectal, heterotopic gastric mucosa causing, (1940) 279

- retinal, after blood transfusion, (1943) 326

- shock due to, (1943) 338

- spontaneous, into rectus abdominis, (1940) 413

- subarachnoid, hydrocephalus following, (1940) 344

- subendocardial, shock, in, (1940) 528

- tourniquet, new type of, (1940) 347

- uterine, functional, stilboestrol in treatment, (1944) 26

- vitamin K and, (1940) 4, 6, 131, 590-2

- vitamins, relation to, (1943) 230, 378

Haemorrhagic

conditions,

- prothrombin deficiency in, (1943) 24

- vitamins and, (1943) 378

deficiency disorders,

- plasma-prothrombin titrations in infants, (1941-2) 241

- vitamin P, treatment with, (1941-2) 241

- diathesis, (1940) 6

- associated with idiopathic steatorrhoea, (1941-2) 192

- pathogenesis and morbid anatomy, (1941-2) 241

- primary non-hereditary, (1941-2) 241

- diseases, (1939) 363; (1941-2) 241; (1944) 246

- dicoumarin in, (1944) 322

- hereditary, (1941-2) 241; (1944) 246

CUMULATIVE INDEX

Haemorrhagic—continued diseases—continued

- new-born, of, (1940) 31, 326, (1943) 230
- vitamin K, antenatal administration of, (1944) 246
- thrombocytopenic purpura, (1939) 362
- pathology, (1939) 363
- vitamin K in relation to, (1940) 590-2
- measles, (1944) 298
- states, (1939) 53, (1940) 31
- prothrombin in, (1940) 31
- vitamin K in, (1940) 31, 131
- telangiectasia, familial, (1941-2) 223
- Haemorrhoids, internal, injection treatment, (1941-1942) 375
- Haemostasis
 - mechanism of, (1941-2) 268
 - rabbit thrombin, use of, (1943) 118
 - vitamins and, (1943) 378, (1944) 405
- Haemothorax
 - spontaneous, (1940) 327
 - traumatic, (1941-2) 72
 - clinical categories and treatment of, (1941-2) 242
- Haemo-tympanum, idiopathic, (1943) 198
- Hair, (1940) 328
 - excessive, removal of, (1940) 328
 - follicles,
 - abnormalities and diseases, (1939) 363, (1941-1942) 243
 - lanugo hair, (1939) 363
 - tumours derived from, (1941-2) 393
 - human, as suture material, (1944) 18
 - permanent waving, hydrogen sulphide poisoning, (1941-2) 410
 - red, and susceptibility to tuberculosis, (1941-2) 414
 - twisted, (1940) 328
- Hair-dye, dermatitis caused by, (1940) 258
- Halibut-liver oil, official preparations of, (1940) 128
- Halisteresis, otosclerosis and, (1943) 181
- Hallucinations, visual, in paraldehyde addiction, (1944) 208
- Hallux valgus, control of post-operative pain, (1940) 302
- Halogens, sensitization to, in dermatitis herpetiformis, (1941-2) 204
- Hamartiosis, disseminated, (1943) 204
- Hamartomas, (1943) 204
- Hamilton-Schwartz test, (1943) 298
- Hamman's disease, (1944) 301
- Hamman's sign, (1944) 302
- Hand
 - diseases, (1940) 329
 - deformities, and, (1941-2) 243
 - ganglion of, (1941-2) 243
 - Heberden's nodes, (1941-2) 243
 - immersion, (1944) 239
 - injuries, treatment, (1944) 246
 - oedema, hysterical, of, (1940) 426
 - osteophytes, (1941-2) 243
 - pain, in acromegaly, (1941-2) 129
 - ringworm, (1941-2) 233
 - tumours, primary, of, (1940) 302
- Hands, preparation of the surgeon's, (1944) 14
- Hand-Schuller-Christian syndrome *See* Schuller-Christian syndrome
- Hanoi's unifoliar cirrhosis, (1941-2) 289
- Harara, (1940) 464
- Hardy, oedematous scleroderma of, (1940) 517
- Hare-lip, cupid's-bow operation, new, (1940) 430
- Hashish, addiction to, (1939) 318
- Hawthorn, in hypertension, (1940) 216
- Hay fever
 - clinical picture, (1944) 126
 - diagnosis, (1944) 126
 - pollen contact on age of onset, effect of, (1941-2) 137
 - pollen extracts and skin sensitivity, (1941-2) 137
 - skin testing in children, (1933) 127
 - treatment,
 - adrenaline in oil, (1940) 161
 - histaminase, (1940) 161
 - oral pollen, (1941-2) 137
 - pollen antigen hydrochloride, (1944) 128

Hay fever—continued treatment—continued

- pollen extract, slow absorbing, (1941-2) 136
- pollen extracts in oil, (1944) 128
- potassium salts, (1940) 161
- Head
 - closed injury, treatment, (1944) 185
 - injury, (1940) 348
 - after-treatment, (1944) 268
 - amniotic membrane, use of, (1940) 348
 - aponeurotic transplantation, (1940) 348
 - cerebral oedema, acute, (1944) 184
 - crash helmets, effects of wearing, (1943) 8, 250; (1944) 270
 - ear involvement in, (1940) 49-53
 - electroencephalography in, (1944) 226, 228
 - encephalography in, (1944) 357
 - euphoria, (1940) 72
 - psychiatric examination in, (1940) 60
 - rehabilitation after, (1943) 178
 - treatment, (1943) 8, (1944) 185
 - wounds,
 - chemotherapy in treatment of, (1940) 10
 - incised and punctured, (1944) 268
- Headache, (1939) 363, (1941-2) 90, 244
 - encephalography in, (1940) 103
 - erythromelalgia of head, (1939) 363
 - hypertension, relation to, (1941-2) 306
 - middle turbinate inflammation cause of, (1939) 364
 - migraine causing, (1941-2) 91, (1944) 247
 - ovarian insufficiency causing, (1940) 329
 - powders, poisoning by, (1941-2) 409
 - spinal injection causing, (1940) 110
 - X-ray therapy, (1940) 110
- Healing, wounds, of, (1941-2) 113
- Hearing
 - airplane noise, effect on, (1940) 206, (1941-2) 36
 - aviators, of, (1941-2) 160, (1943) 141
 - defects, relation to speech defects, (1940) 535
 - diplacusis, (1940) 283
 - 'hard of hearing', test of, (1944) 193
 - myastoidectomy, effect of, (1940) 285
 - mechanism of, (1944) 193
 - physiology of, (1944) 87
- Hearing aids, (1939) 100
 - instruments, (1939) 100
 - lip reading, (1939) 107
 - prescription of, (1939) 102
 - provision of, (1939) 104
- Heart
 - abnormalities, congenital, (1941-2) 246, (1943) 1
 - acetylcholine, effect of, (1941-2) 333
 - athletes, of, (1940) 204
 - auscultation, portable amplifier for, (1941-2) 245
 - benzedrine, effects of inhalation, (1940) 449
 - beri-beri, (1941-2) 5
 - block,
 - Adams-Stokes attack and the electrocardiogram, (1941-2) 246
 - bundle-branch, relation to cardiac enlargement, (1941-2) 150
 - congenital, (1940) 331
 - digitalis in, (1940) 191
 - thyroid intoxication causing, (1940) 315
 - bullet lodged in, (1941-2) 249
 - carcinoma, secondary to carcinoma of bronchus, (1941-2) 294
 - chambers, visualization of, (1940) 503
 - compression, treatment, (1940) 337
 - dextrocardia, (1941-2) 246
 - digiland, effect of, (1941-2) 334
 - digoxin, effect of, (1940) 135
 - dilatation, hypertension causing, (1944) 250
 - diphtheria, in, (1944) 205
 - disease, (1941-2) 44, 244, (1944) 247-51
 - advances in knowledge of, (1940) 5
 - anxiety neurosis and, (1944) 341
 - aortic valve diseases, (1939) 370
 - stenosis, (1939) 370
 - congenital, (1939) 364, (1940) 331, (1941-2) 246, (1943) 233, (1944) 248
 - cardiac pentad, (1939) 365
 - cerebral abscess in relation to, (1941-2) 174
 - electrocardiography in, (1943) 233

CUMULATIVE INDEX

Heart—continued

disease—continued

congenital—continued

- Fallot's tetralogy, (1939) 364
- heart-block, (1940) 331
- hypertrophy, idiopathic, (1940) 331; (1943) 233
- patent ductus arteriosus, (1939) 364; (1943) 233
- endocarditis, malignant, (1939) 368
- acute bacterial, pathology of, (1939) 369
- subacute bacterial, (1939) 368
- gonococcal, (1939) 368
- splenectomy, (1939) 368
- sulphanilamide, (1939) 369
- heart failure, (1939) 370
- digilamid in, (1939) 371
- digitalis in, (1939) 371
- gangrene, peripheral, complicating, (1939) 370
- mitral valve diseases, (1939) 369
- mitral stenosis with ball thrombus in left auricle, (1939) 369
- myocardial, (1939) 367
- acute infarction, (1939) 367
- stab wounds, (1939) 368
- treatment, foetal-heart hormone in, (1939) 367
- tumours, (1939) 367
- myxoedema, association with, (1943) 286
- ouabain in treatment, (1944) 321
- pericardial,
 - chronic constructive pericarditis (Pick's disease), (1939) 365
 - kymography, (1939) 365
 - partial pericardiectomy, (1939) 367
 - pericardiolysis technique, (1939) 366
- pulmonary, (1943) 240
- recruits, in, (1941-2) 44
- rheumatic, (1940) 332
- children, in, (1939) 365
- aetiology, (1939) 365
- diagnosis and treatment, (1943) 234
- syphilitic aortic valvulitis combined with, (1943) 238
- rheumatoid arthritis, associated with, (1941-2) 154
- soldiers, in, (1940) 329-31
- surgical treatment of, (1940) 15, 337-9
- survey of, (1939) 20
- syphilis, congenital, incidence of, (1941-2) 403
- thyroidectomy for, (1940) 338
- traumatic, (1941-2) 270
- vitamin B deficiency and, (1941-2) 423
- disordered action of, (1941-2) 2
- disorders,
 - coramine, effects of, (1941-2) 334
 - hypertonic glucose injections in, (1941-2) 340
 - pitressin, effects of, (1941-2) 336
 - respiration in, (1941-2) 334
- drugs acting on, (1940) 135
- enlargement,
 - children, in, (1943) 233
 - relation of bundle-branch block to, (1941-2) 150
- examination of, (1939) 57-9, (1941-2) 244, (1944) 247
- soldiers, in, (1940) 329-31
- failure, (1941-2) 253, (1944) 250
- blood viscosity in, (1940) 337
- calcium gluconate in, (1940) 337
- cardiac hypertrophy, association with, (1943) 241
- chemical changes in myocardium, (1943) 240
- congestive, (1943) 241
- prognosis of, (1941-2) 253
- convallan in treatment, (1940) 338
- desoxycorticosterone, administration of, after, (1941-2) 132
- digitalis, action of, (1940) 337
- hypertension causing, (1944) 250
- physiology, (1944) 250
- treatment of, (1939) 60; (1940) 129, 337; (1941-1942) 253
- calcium gluconate, (1941-2) 254
- digitalization, single dose, (1944) 250

Heart—continued

failure—continued

treatment of—continued

- medical therapy and general management, (1941-2) 253
 - mercurial diuretics, (1941-2) 253
 - ouabain and digitalis, (1941-2) 254
 - vitamin B₁ therapy, (1940) 129; (1941-2) 254
 - fatigue, tests of, (1943) 232
 - fear on, effect of, (1941-2) 149
 - foreign bodies, (1940) 333; (1941-2) 249
 - functional capacity and hypertension, (1941-2) 245
 - great vessels, transposition of, (1941-2) 248
 - heat-stroke, cardiac changes in, (1940) 339
 - hypertrophy, (1943) 240
 - congenital idiopathic, (1940) 331
 - hypertension causing, (1944) 250
 - idiopathic, in infants and children, (1943) 233
 - injuries, (1940) 334
 - non-penetrating, (1941-2) 270
 - kymography of, (1940) 101
 - lanatoside C, effect of, (1941-2) 337
 - leiomyosarcoma, primary, (1943) 235
 - leptazol, effect of, (1941-2) 337
 - magnesium glutamate, effect of, (1940) 317
 - mega syndromes and, (1944) 85
 - myal thrombi, (1941-2) 218
 - murmurs, diminished attention paid to, (1940) 5
 - myasthenia gravis, in, (1944) 306
 - nicotine, effect of, (1941-2) 409
 - non-penetrating traumatic injuries, (1941-2) 270
 - recruits, (1941-2) 2
 - respiratory failure, treatment of, and, (1939) 164
 - resuscitation after cardiac arrest, (1943) 326
 - rheumatic disease of, (1940) 332, (1941-2) 252
 - children, mortality in, (1944) 248
 - diagnosis, (1940) 332
 - haemolytic streptococci, recovery of, (1941-2) 377
 - heart lesions, (1940) 332
 - pregnancy, in, (1944) 335
 - two-step test, (1941-2) 378
 - right-sided hypertrophy, (1941-2) 252, 291, (1943) 240
 - roentgen-cinematography of circulation, (1944) 355
 - septal defect, atrial, (1943) 1
 - sex hormones on, effect of, (1941-2) 381
 - situs inversus, complete, with visceral pain, (1941-1942) 246
 - soldier's, (1941-2) 2, (1943) 231
 - sounds, recording of, (1941-2) 245
 - stab wounds, (1940) 334, (1943) 235
 - strophanthin, effect on, (1940) 135
 - surgery of, (1943) 13
 - syphilis of, (1943) 238
 - hypertension, and, in, (1943) 239
 - tumours, myocardial changes resulting from, (1943) 235
 - valvular disease, (1941-2) 252
 - vitamin B₁ deficiency and, (1940) 586
 - war, and, (1943) 231
 - wounds, (1940) 334; (1941-2) 249
 - non-penetrating, (1944) 273
 - coronary thrombosis due to, (1944) 140
 - wounds and injuries, (1943) 1, 13, 235
 - diagnosis and treatment, (1943) 236
 - electrocardiographic changes, (1943) 236
 - X-ray examination, (1940) 503
- ## Heat
- effect on shock, (1941-2) 387
 - prickly, (1944) 335
 - reduction by drugs, (1941-2) 339
 - regulation, hypothalamus and, (1940) 65
 - rheumatism treated with, (1941-2) 229
 - stroke,
 - cardiac changes in, (1940) 339
 - pathology and morbid anatomy, (1940) 339
- ## Heberden's nodes, (1941-2) 243
- ## Helium-oxygen
- asphyxiated infants, in treatment of, (1941-2) 156
 - asthma, in, (1939) 234
 - laryngitis, inhalation in treatment of, (1941-2) 281

CUMULATIVE INDEX

- Helium-oxygen—continued**
 mixture, effect on voice, (1941-2) 335
 therapy, aero-otitis media, in, (1941-2) 182
- Hellebore, green.** *See* *Veratrum viride*
- Helmets**
 armour, and, (1943) 8
 crash, (1944) 270
- Hemicellulose hydrogels, effect on bulk of stools,**
 (1944) 190
- Hemiparesis, migraine associated with, (1940) 408**
- Hemiplegia**
 anosognosia and autotopnosia in, (1943) 241
 imperception of, (1943) 75
 post-operative, associated with hypotension,
 (1941-2) 167
 post-partum obstruction of central retinal artery
 associated with, (1940) 510
 sodium diphenylhydantoinate causing, (1940)
 293
 thalamic lesion causing, (1940) 64
- Hemiprostectomy for unilateral adenomatous en-
 largement, (1943) 313**
- Heparin, (1941-2) 12**
 action of, (1940) 137
 anticoagulant action, (1940) 136
 blood platelets, effects on, (1944) 159
 cavernous sinus thrombophlebitis treated with,
 (1941-2) 408
 embolism, arterial, treated with, (1940) 286
 endocarditis,
 infective, in, (1940) 137
 subacute bacterial, treated with, (1940) 336,
 (1941-2) 251, (1943) 237
 sulphapyridine, and, (1941-2) 251
 peritoneal adhesions, in, (1940) 452
 post-operative thrombosis, use in prevention of,
 (1941-2) 335
 prevention of blood clotting, (1941-2) 335
 pulmonary embolism treated with, (1940) 395,
 (1941-2) 296, (1944) 15
 retinal venous thrombosis treated with, (1941-2)
 376
 surgery and thrombosis, use in, (1941-2) 335
 therapeutic use, (1940) 137
 thrombophlebitis treated with, (1941-2) 296
 thrombosis, in, (1940) 137, 582
 unit, (1940) 137
 varicose veins, in, (1944) 399
- Hepatectomy, partial, effects of colchicine after,
 (1941-2) 334**
- Hepatex, pink disease treated by injection of, (1944)
 330**
- Hepatic**
 cirrhosis *See* *Liver, cirrhosis*
 function, sulphonamides, and, (1940) 458
- Hepatitis**
 acute,
 aspiration biopsy of liver in, (1940) 28
 catarrhal jaundice and, (1940) 28
 epidemic forms, (1944) 289
 mild forms, (1944) 289
 operation for appendicitis, after, (1941-2)
 149
 chronic, (1940) 387; (1943) 268. *See also* *Liver,
 cirrhosis*
 abdominal venous thrill, (1941-2) 288
 alcoholism and, (1941-2) 135
 morbid anatomy, (1944) 290
 pathogenesis, (1944) 290
 pernicious anaemia, with, (1943) 268
 predominant jaundice, with, (1941-2) 289
 treatment by diet and vitamin B complex,
 (1943) 268
 vitamin deficiency, in, (1943) 268
 infective, (1943) 267; (1944) 33, 62, 289
 aetiology, (1944) 33
 incubation period, (1944) 34
 pathogenesis, (1944) 34
 symptoms, (1944) 34
 treatment, (1944) 35
 virus agent, (1944) 34
 toxic. *See* *Hepatitis, infective*
- Hepato-lenticular degeneration, (1939) 372**
 clinical picture and Kayser-Fleischer ring, (1939)
 372
- Hepato-lenticular degeneration—continued**
 corneal pigment (Kayser-Fleischer zone), (1943)
 241
 hepatic cirrhosis in, (1943) 242
- Hepato-lenal fibrosis, (1941-2) 398; (1943) 351**
- Hepatomegaly**
 dwarfism, and, complicating diabetes mellitus,
 (1943) 35
 glycogenic, associated with diabetes mellitus,
 (1940) 263
- Hepatonephrosis, (1940) 357**
- Hepato-renal**
 disease, pyridine causing, (1944) 229
 syndrome, (1940) 356
- Hepatosi, pre-cirrhotic, in alcoholism, (1941-2)
 135**
- Hepato-splenomegaly-lipoidosis, of Burger and
 Grutz, (1941-2) 287**
- Hepato-trophic properties of sex hormones, (1941-
 1942) 381**
- Hereditary**
 absence of uterus, (1940) 577
 cranio-facial dysostosis, (1943) 295
 ectodermal dysplasia, (1941-2) 147
 haemorrhagic disorders, (1941-2) 241
 oedema, (1941-2) 318, (1943) 293
 telangiectasia with visceral involvement, (1941-2)
 223
- Heredity**
 cancer, in, (1939) 270
 constitution, and, (1941-2) 254
 disseminated sclerosis, in, (1940) 277
 ichthyosis vulgaris, in, (1943) 246
 leprosy, (1940) 379
 psychoneurosis, in, (1943) 65
 pulmonary tuberculosis, in, (1943) 62
 skin malformations and, (1943) 344
 tumours in twins, (1941-2) 254
- Hermaphroditism**
 andric and gynec influences in, (1943) 212
 false. *See* *Pseudo-hermaphroditism*
 gout associated with, (1943) 226
 soldiers, in, (1943) 10
 strangulated, (1943) 11
 true, (1940) 576
- Hernia, (1939) 372, (1941-2) 255**
 amniotic, (1941-2) 255
 diaphragmatic, (1940) 268
 eversion, (1941-2) 255
 external abdominal, (1940) 339, 353, (1941-2)
 255
 trauma and, (1940) 339
 fascial suture, (1940) 340
 hepatic disease and ascites associated with, (1941-
 1942) 255
 inguinal,
 cord transplantation in, (1941-2) 255
 direct form of, (1939) 372
 new operative technique for, (1941-2) 255
 injection treatment, (1939) 373, (1940) 12, 340
 end-results of, (1941-2) 255
 intestinal obstruction caused by, (1940) 353
 old age, in, (1940) 340
 radical cure of, (1940) 12
 recurrent, (1940) 341
 tibialis anterior muscle, of, (1944) 305
 trauma and, (1940) 339
 treatment of, (1940) 12, 340, (1941-2) 14
 fascial suture, (1940) 340
 injection therapy, (1940) 340
 surgical, (1940) 341
 umbilical cord, in, (1941-2) 255
- Herniotomy, old age, in, (1940) 341**
- Herpes, (1941-2) 255**
 labialis,
 sulphapyridine and T.A.B. vaccine causing,
 (1943) 242
 treated with spiritus vini rectificatus, (1941-2)
 256
 recurrent-traumatic, (1940) 341
 simplex, (1939) 373
 aetiology, (1939) 373
 arsenical dermatitis, associated with, (1941-2)
 256
 artificial pyrexia, causing, (1940) 202

CUMULATIVE INDEX

Herpes—continued

simplex—continued

differential diagnosis and pathology, (1939) 374
moccasin snake venom treatment, (1939) 374,
(1941-2) 256

zoster, (1939) 374

aberrant vesicles, (1941-2) 256
aetiology, (1941-2) 255
chicken-pox, association with, (1940) 246,
(1941-2) 255
clinical picture, (1941-2) 256
cornea of, (1943) 179
encephalitis complicating, (1939) 374
mumps complicated by, (1941-2) 309
ophthalmicus, convalescent blood in treatment,
(1941-2) 198
paralysis following, (1941-2) 256
procaine injections, (1939) 374
treatment, (1941-2) 256
 anaesthetic infiltration, (1941-2) 256
 vitamin B₁₂, (1939) 374
 X-ray of the spine, (1941-2) 256
varicella, association with, (1943) 242

Hesperidin See Vitamin P

Heterophoria, (1940) 546

Hexamine, tetanus treated with, (1941-2) 407

Hexamine insulin, (1943) 34

Hexanastab, hexobarbitone soluble, official name for,
(1940) 127

Hexazole, (1941-2) 79, (1944) 110 See also Cardiazol
Hexobarbitone soluble, (1940) 127 See also Evipan
soluble

 basal hypnotic, as, (1941-2) 142

 blood-oxygen capacity after, (1941-2) 142

Hexoestrol, (1940) 132, 522, (1943) 98, 336 See also
Hormones, sex

Hexylresorcinol, *trichomonas vaginalis* treated with,
(1941-2) 429

Hibernation, cancer treated by, (1941-2) 184

Hidradenitis suppurativa, (1939) 320

High-frequency currents, effect on the body, (1941-
(1942) 217

Hip

dislocation of, (1939) 314

fractures,

 treatment, (1944) 20

 Smith-Petersen nail, (1944) 20

osteochondritis dissecans of, (1940) 360

osteotomy for osteoarthritis of, (1939) 391

tuberculosis of, (1939) 391

Hippuric acid,

excretion,

 hyperthyroidism, in, (1941-2) 236

 schizophrenia, in, (1940) 489

test, (1944) 288

 liver function, of, (1940) 116, 386

 surgical prognosis, use in, (1944) 287

 thyroid diseases, in, (1940) 317

Hirsuties

adrenal hypertrophy causing, (1941-2) 243

endocrine therapy, (1940) 328

Histaminase

allergic conditions, in, (1940) 163

 cold allergy treated with, (1940) 163

 dermatoses, allergic, in, (1940) 163, (1941-2) 137

 genito-urinary allergy treated with, (1940) 164

 hay fever treated with, (1940) 161

 peptic ulcer treated with, (1940) 441

 serum sickness, in, (1939) 201

 skin tests in allergic cases, (1941-2) 136

 vasomotor rhinitis treated with, (1940) 162

Histamine

allergic reactions, role in, (1941-2) 136

 azoprotein, in treatment of allergic diseases,
(1943) 112

 blood variations in allergic diseases, (1943) 112

 dermatoses, atopic, treated with, (1943) 112

 iontophoresis, for varicose ulcer, (1940) 581

 -like substance in shock, (1941-2) 386

 Ménière's syndrome, in, (1940) 584; (1941-2) 422,
(1943) 377

 peptic ulcer, relation to, (1941-2) 326

 phosphate, injections, effect on pressure of cere-
brospinal fluid, (1941-2) 188

 rheumatoid arthritis treated with, (1940) 198

Histamine—continued

 schizophrenia treated with, (1939) 503

 shock, role in, (1941-2) 386

 vitamin C, effect of, on muscle response to, (1941-
(1942) 425

Histone zinc insulin, (1943) 34

Histoplasma capsulatum, (1941-2) 257; (1943) 243

Histoplasmosis, (1940) 342, (1941-2) 257

 clinical course and histological observations,
(1944) 251

 clinical picture, (1941-2) 257

 infant, occurrence in, (1941-2) 257

 lung, of, (1943) 243

 morbid anatomy, (1944) 251

Hoarseness, functional, (1944) 219

Hodgkin's disease, (1939) 375, (1941-2) 257, (1944)
251-4

 abdominal, (1941-2) 258

 aetiology, (1940) 342

 anaemia, hyperchromic macrocytic, in, (1940)
343

 bone lesions, (1944) 252

 breast, of, (1944) 252

 brucella infection associated with, (1941-2) 257

 clinical picture, (1940) 342, (1944) 251

 course and prognosis, analysis of, (1943) 243

 diagnosis and differential diagnosis, (1940) 343,
(1941-2) 258, (1943) 244

 gastric

 lesions, (1940) 343

 mucosa, in, (1939) 375

 Gordon's test, (1939) 375

 reliability of, (1941-2) 258

 haemoptysis in, (1941-2) 258

 intrathoracic, (1941-2) 258

 mycosis fungoides and, (1943) 286

 pregnancy, in,

 clinical course after X-ray irradiation, (1944)
252

 prognosis, (1939) 375, (1940) 342

 radiological examination in diagnosis, (1943) 244

 recent observations in, (1944) 253

 respiratory tract, (1941-2) 258

 skin manifestations, (1944) 251

 stomach, in, (1940) 343

 treatment

 irradiation, by, (1943) 244

 regional X-ray bath, (1940) 105

 X-ray therapy, (1939) 375, (1940) 105, 344,
(1944) 252

 twins, in, (1943) 243

 urinary bladder, in, (1941-2) 258

Hog's stomach, gastritis, chronic atrophic, treated
with, (1940) 312

Holmgren wool-test for colour blindness, (1940) 60

Hologynic inheritance, of ichthyosis vulgaris, (1943)
246

Homatropine-paredrine, pupil, effect on, (1940) 449

Homeless, carc. of, (1944) 8

Homosexuality, (1944) 77

 genetics of, (1940) 60

 leptazol therapy, (1941-2) 385

 male, endocrine basis, (1940) 527

Honey in diet, composition of, (1939) 382

Hormodendrum pediosai, (1941-2) 233

Hormones, (1941-2) 335 See also under names of
the various hormones

 Addison's disease, adrenal cortical, in, (1939)
190

 mammary cancer, in relation to, (1939) 190

 adrenal glands, (1944) 53

 alopecia, in, (1940) 165

 androgens, (1941-2) 384

 anterior pituitary, (1941-2) 382

 growth hormone, (1943) 302

 breast, in relation to, (1939) 264

 cerebral circulation, effect on, (1940) 56

 cervicitis, influence in, (1940) 22

 climacteric, in, (1940) 248

 desoxycorticosterone, (1941-2) 383

 acetate, (1941-2) 335

 dysmenorrhoea, in, (1940) 283

 endometrial extract, (1941-2) 383

 Fallopian tubes, in non-patency of, (1940) 298

 foetal heart, in heart disease, in, (1939) 367

CUMULATIVE INDEX

Hormones—continued

- gonadotrophic, (1944) 369
- antigonadotrophic activity in man, production of, (1940) 520
- cysteine, effect of, on, (1940) 520
- male sub-fertility, in, (1939) 157
- oestradiol benzoate, effect of, on gonadotrophic activity of pituitary, (1940) 521
- psychiatry, role in, (1941-2) 364
- sterility, male, treated with, (1940) 543
- undescended testis treated with, (1940) 551
- growth (antitumour-growth), (1939) 108
- hirsuties, in, (1940) 328
- ketosteroids, neutral, rate of excretion of, (1941-2) 384
- lactogenic, (1939) 109, (1944) 52
- male sex, (1940) 523-7
 - abortion induced by, (1940) 142
 - assay, method of, (1940) 523
 - clinical uses, (1940) 525-7, (1941-2) 384
 - men, in, (1940) 525
 - women, in, (1940) 20, 525
 - gynaecology, in, (1939) 35
 - hypogonadism treated with, (1940) 525
 - kidneys, effects on, (1940) 524
 - mental disorders treated with, (1940) 525
 - women, biological effects in, (1940) 525
- meno-metrorrhagia, in, (1940) 407
- mental disease, in, (1940) 55
- migraine, in, (1940) 409
- oestradiol, (1941-2) 335, 382
- oestrogenic, (1940) 20, 521-3, (1941-2) 382 *See also* Oestrogens
- otosclerosis, in, (1940) 255
- ovarian and synthetic oestrogenic substances, (1941-2) 382
- ovarian follicle stimulating, (1941-2) 382
- ovaena, in, (1940) 429
- parathyroid, detection of, (1943) 298
- perandren, (1941-2) 382
- pitressin, (1941-2) 336
- pituitary, (1941-2) 351
 - gonadotrophic extracts, (1941-2) 336
- pregnancy, in, (1941-2) 357
- toxæmias, in, (1940) 108
- pregnanediol *See* Pregnanediol
- prematurity, in, (1940) 482
- progesterone, (1941-2) 384
- progynon, (1941-2) 382
- prostatic enlargement, in, (1940) 14
- schizophrenia, in, (1940) 495
- sex, (1940) 131, 520-7, (1941-2) 381, (1943) 332
 - See also* Sex hormones
 - abortion and, (1943) 15
 - blood pressure, relation to, (1941-2) 382
 - cancer, in relation to, (1940) 7
 - cancer tissue, effect on, (1941-2) 183
 - carcinogenic action of, (1941-2) 183
 - corpus luteum, (1943) 95, 333
 - excitation in children, (1941-2) 382
 - hepatotrophic and cardiotropic properties of, (1941-2) 381
 - homosexuality, male, and, (1940) 527
 - kidneys, effects on, (1940) 524
 - lactogenic, (1943) 332
 - liver and heart, effect on, (1941-2) 381
 - male, (1941-2) 384
 - malignant disease treated with, (1941-2) 184
 - men, actions in, (1943) 335
 - menstrual and climacteric disorders, in, (1941-2) 384
 - ovarian, (1943) 333
 - ovary, effect on, (1941-2) 22
 - psychiatry, role in, (1941-2) 364
 - stilboestrol *See* Stilboestrol
 - subcutaneous implantation of tablets, (1940) 520
 - uterine bleeding, effect on, (1941-2) 21
 - women, actions in, (1943) 333, 336
- spondylitis deformans, in, (1940) 200
- stilboestrol, (1941-2) 383
- testosterone, (1941-2) 382, 384
- therapy, (1943) 19, 94-8, 307, 332-7
 - allergic diseases, in, (1944) 125
 - amenorrhoea, in, (1943) 97, 114, 334
 - trophic rhinitis, in, (1939) 90

E.M.S. II

Hormones—continued therapy—continued

- breast, carcinoma of, in, (1943) 164
- dysmenorrhoea, in, (1943) 97, 336, (1944) 211
- enlarged prostate, in, (1939) 158
- eunuchism and hypogonadism, (1941-2) 384
- gynaecology, in, (1944) 26
- impotence, in, (1943) 335
- infantilism, in, (1943) 197
- involutional
 - melancholia, in, (1941-2) 365
 - psychoses, in, (1944) 347
- lactation, inhibition of by, (1943) 335
- male, in, (1943) 335
- menopausal
 - disorders, in, (1941-2) 190
 - symptoms, in, (1943) 20, 98, 334
- menstrual and climacteric disorders, in, (1941-2) 384, (1944) 369
- mental disorders, in, (1941-2) 81
- obesity in children, in, (1941-2) 130
- ovary, effect on, (1943) 20
- papilloma, laryngeal, in, (1943) 43
- prostatic enlargement, in, (1944) 93
- pyelo-ureteral dilatation produced by, (1943) 19
- undescended testis, in, (1940) 14, (1941-2) 5, 406
- vaginitis, in, (1941-2) 429
- thyroid gland, of, (1943) 307
- thyroidotrophic, (1941-2) 382
- ureter during pregnancy, influences on, (1944) 23
- uterine inertia treated with oestrogenic, (1939) 31
- Horns, cutaneous, (1943) 345
- Hospitals
 - control of dust in, (1941-2) 185
 - equipment, disinfection of, and control of infection, (1941-2) 185
 - irradiation of air in, (1941-2) 130
- Hostility, manic-depressive psychosis, role in, (1944) 346
- Housing, in war-time, (1944) 8
- Houssay phenomenon, man, in, (1940) 262
- Human
 - factor in medicine, (1940) 8
 - oil, adherent scars treated with injections of, (1939) 386
- Humerus
 - boils, acute acromial, (1940) 300
 - epicondylitis, (1940) 300
- Hunger
 - morbid, and periodic somnolence, (1943) 318
 - oedema, (1943) 189
- Hunner's ulcer of bladder, (1944) 94
- Hutchinson's teeth, (1944) 382
- non-syphilitic, in, (1941-2) 202
- Hydatid
 - cyst,
 - bone, of, (1941-2) 259
 - ilium, of, (1941-2) 259
 - kidney, of, surgical treatment, (1941-2) 258
 - uterus, of, (1941-2) 419
 - disease, (1939) 376, (1941-2) 258
 - Cason's method of diagnosis, (1939) 376
 - incidence in Iceland, (1939) 376
 - labour obstructed by, (1939) 394
 - vertebral column, in, (1939) 376
- Hydatidiform mole, (1941-2) 190
- chorionepithelioma and, (1940) 246
- malignancy, criteria of, (1940) 247
- quantitative Friedman test in, (1940) 246
- Hydrargyria
 - maligna, (1941-2) 224
 - mitis, (1941-2) 224
 - simplex, (1941-2) 224
- Hydration, toxæmias of pregnancy in, (1940) 480
- Hydrocarbons, chlorinated, poisoning by, (1941-2) 411
- Hydrocele
 - canal of Nuck, of, (1941-2) 330
 - injection treatment, final results of, (1941-2) 406
 - renal, (1939) 394
 - renis, (1943) 258
 - treatment, quinine dihydrochloride and urethane injections, (1943) 360
- Hydrocephalus
 - otic, (1940) 66, 345

CUMULATIVE INDEX

Hydrocephalus—continued
 subarachnoid haemorrhage and, (1940) 344
 toxic, (1940) 66
 unilateral internal, (1941-2) 259
Hydrochloric acid
 calcification of bone, in relation to, (1939) 314
 collargol test, and, (1941-2) 188
Hydrocyanic acid, poisoning by, (1944) 384
Hydrofluoric acid
 burns, treatment of, (1939) 267
 osteosclerosis caused by, (1940) 560
Hydrogen
 ion concentration, vagina and cervix, of, (1940) 22
 sulphide, poisoning during permanent wave, (1941-2) 410
Hydrometrocolpos in infants, (1941-2) 430
Hydronephrosis
 horseshoe kidney, of, (1943) 258
 massive, (1943) 259
 perirenal, (1943) 259
 treatment, (1940) 364
 preliminary nephrostomy, (1944) 277
 ureter, tumour of, primary benign, (1943) 258
Hydrosulphosol, burns treated with, (1943) 305
Hydrotherapy, (1939) 376, (1941) 244
 hot-water baths in rheumatism, (1939) 376
 mud baths in cardiovascular disease and poly-
 arthritis, (1939) 377
 sulphur and sea water baths in cardiovascular
 disease and polyarthritis, (1939) 377
Hydroxyethylapocupreine
 dihydrochloride, pneumonia treated with sulpha-
 pyridine and, (1940) 472
 pneumonia treated with, (1941-2) 354
8-Hydroxyquinoline, impetigo contagiosa treated
with, (1940) 346
Hygiene, industrial, (1944) 259
Hymen, imperforate, with haematocolpos, (1940) 592
Hyoscine
 convulsion therapy, use in, (1941-2) 79
 spasm, use in, (1939) 165
Hyperaesthesia, cutaneous abdominal, in dyspeptics,
(1941-2) 215
Hyperchlorhydria
 aetiology, (1941-2) 259
 drugs and diet, treatment with, (1943) 245
 fruit juice, effect on, (1941-2) 259
 magnesium trisilicate in treatment, (1939) 377
Hypercholesterolaemia, arcus senilis associated with,
(1939) 293
Hyperemesis
 gravidarum,
 adrenal cortex therapy, (1940) 479
 aetiology of, (1941-2) 358
 ocular complications in, (1943) 17
 treatment,
 husband's blood, injection of, (1944) 333
 vitamins B₁ and B₁₂, (1944) 334
 hiemis, (1941-2) 232
Hyperidrosis, surgery of, (1939) 378
Hyperinsulinism, (1943) 245
Hyperkeratosis, palms and soles, of, (1941-2) 191
Hypernephroma, (1941-2) 277
 metastases simulating aneurysms, (1941-2) 133
 ovary, of, (1940) 429
 renal, and virilism, (1941-2) 133
Hyperparathyroidism, (1941-2) 322
 children, in, (1940) 433
 clinical
 features, (1941-2) 322
 types, (1941-2) 322
 dental symptoms, (1941-2) 322
 Hamilton-Schwartz test, (1943) 298
 morbid anatomy, (1941-2) 323
 mouth, condition of, (1941-2) 322
 renal
 calcification in, (1941-2) 144
 insufficiency complicating, (1941-2) 323
 secondary to acromegaly, (1943) 105
 spinal osteoporotic type, (1941-2) 322
 Werner's syndrome, (1943) 298
Hyperpituitarism, gigantism, (1940) 467
Hypertension
 aetiology, (1940) 215; (1944) 161
 adrenal tumours causing, (1943) 150

Hypertension—continued
 arrhythmia in, (1940) 193
 arterial,
 antiotonin, effects of, (1943) 150
 mental disorders, relation to, (1943) 134
 blood pressure, effect on subsequent course, (1940)
 213
 body build, relation to, (1941-2) 166
 carbon monoxide poisoning causing, (1940) 212
 cardiac hypertrophy and dilatation caused by,
 (1944) 250
 cold-pressor reaction, (1940) 216
 course and prognosis, (1944) 160
 eclampsia and pre-eclampsia, after, (1940) 17
 electrocardiogram in, (1941-2) 245
 erythraemia, in, (1944) 231
 essential, (1939) 248, (1940) 211-5
 aetiology, (1940) 211, 214, (1941-2) 165; (1944)
 160
 angiotonin, effects of, (1943) 149
 anti-pressor substance, (1943) 149
 ischaemic kidney, (1943) 1, 71, 153
 nutrition, sub-optimal, as causal factor,
 (1943) 149
 renal disease, relation to, (1943) 149
 childhood, in, (1941-2) 164
 degrees of fluctuation in, (1941-2) 165
 heredity, (1940) 212
 pathology and pathogeny of, (1940) 212
 pituitary, posterior, relation to, (1940) 211
 pregnancy, (1944) 334
 toxaemia and, (1943) 16, 312
 supradiaphragmatic splanchnectomy, (1941-2)
 164
 sympathetomy, (1944) 160
 urinary pressor principle, (1940) 211
 functional capacity of heart and, (1941-2) 245
 Goormaghtigh cells, (1944) 161
 heart in combined syphilis and, (1943) 239
 heredity, (1940) 212
 historical review of, (1943) 152
 incidence of pyelonephritis and, (1944) 310
 influence of doctor on hypertensive patients,
 (1941-2) 164
 intrarenal pelvis and, (1944) 161
 kidney, hypertrophy of, (1941-2) 215
 malignant, (1941-2) 164, (1943) 71
 migraine and headaches, relation to, (1941-2) 306
 nephritis, relation to, (1941-2) 312, (1943) 71;
 (1944) 310
 nephrotic syndrome with, in diabetes mellitus,
 (1941-2) 205
 operations for, (1939) 19, 26
 paroxysmal arterial, with adrenal medullary
 tumour, (1939) 193
 pathology and pathogeny of, (1940) 212
 peripheral resistance, nature of, (1940) 216
 pituitary, posterior, relation to, (1940) 211
 pregnancy,
 during, (1949) 30
 toxaemias of, and, (1941-2) 18
 prognosis, (1940) 215
 pyelonephritis and, (1940) 212
 renal
 disease associated with, (1941-2) 165
 chemotherapy, (1941-2) 165
 metabolic activity of kidneys, (1941-2) 165
 pyelonephritis, (1941-2) 165
 treatment with depressor renal extract, (1941-
 1942) 166
 injury in pyelonephritis and, (1940) 212
 ischaemia and, (1941-2) 2
 treatment, (1943) 72, 151
 acetyl- β -methylcholine, (1940) 213
 Crataegus oxyacantha, (1940) 216
 diet, (1943) 151
 irradiation of pituitary and adrenals, (1943)
 152
 potassium thiocyanate, (1940) 213
 fatal poisoning by, (1944) 384
 sulphur, (1940) 214
 surgical, (1939) 61, (1940) 15, 214; (1943) 72,
 151
 thiocyanates, (1943) 151
 anabolin, compared with, (1943) 152

CUMULATIVE INDEX

- Hypertension—*continued*
treatment—*continued*
ureteral dilatation, (1943) 152
X-ray therapy, (1940) 214
unilateral renal disease, in, (1943) 150
vascular, survey of, (1939) 19
vitamin B deficiency in, (1944) 161
- Hyperthyroidism
familial periodic paralysis associated with, (1943) 298
galactose test in, (1940) 316
hippuric acid,
excretion of, in, (1941–2) 236
test, (1940) 317
magnesium glutamate, in, (1940) 317
masked, diagnosis of, (1943) 224
menopause, associated with, (1940) 247, (1941–2) 190
mental disease, in, (1943) 316
myasthenia gravis, relation to, (1940) 416; (1943) 284
recurrence after subtotal thyroidectomy, (1943) 224
thyroid, adenocarcinoma of, and, (1943) 224
- Hypertonia, pyramidal, haematoporphyria in treatment of, (1940) 415
- Hypertonic
sodium sulphate, wound dressing, as, (1940) 351
solutions, effect on kidneys, (1939) 473
- Hypertrichosis
female, in, adrenal hypertrophy causing, (1941–2) 243
mental deficiency associated with, (1939) 431
- Hyperuricaemia, alkaptonuria associated with, (1944) 124
- Hyperventilation
anxiety states, in, (1940) 485
aviation, in, (1941–2) 159, (1943) 140
- Hypervitaminosis C, (1940) 588
- Hypnosis, evipan, in investigation of neuroses, (1941–2) 259
- Hypnotics, (1940) 135, (1943) 64
- Hypnotism, (1941–2) 259
speech defects treated by, (1940) 536
uses of, (1939) 378
- Hypoaminoacidaemia in children with nephrotic crisis, (1940) 421
- Hypochlorite, electrolytic
burns treated with, (1941–2) 180
wounds treated with, (1943) 249
- Hypochromic
anaemia *See* Anaemia, hypochromic
deficiency anaemias, (1941–2) 139
- Hypodermic syringes, transmission of malaria by, (1941–2) 301
- Hypodermoclysis, administration of sulphapyridine by, (1940) 460
- Hypogastric plexus
superior,
anatomy, (1944) 83
plexus morphology, (1944) 83
surgical anatomy, (1944) 84
- Hypoglycaemia, (1943) 35, 245, (1944) 254
alcoholism, acute, causing, (1944) 123
atrophy of adrenals and, (1941–2) 260
brain lesions in, (1944) 255
clinical picture, (1943) 35
fatal, (1944) 255
hyperinsulinism, and, (1939) 378
artificial hypoglycaemia, morbid anatomy of, (1939) 378
functional hyperinsulinism, partial pancreatectomy in, (1939) 379
spontaneous hypoglycaemic encephalopathy, (1939) 379
morbid anatomy, (1944) 254
nervous symptoms of, (1940) 119
pancreatic lesions causing, (1944) 254
pathology, (1943) 36
sequelae, (1943) 36
spontaneous, (1941–2) 260, (1943) 245, (1944) 255
Simmonds's syndrome, in, (1941–2) 390
treatment, (1943) 36, (1944) 255
- Hypoglycaemic shock therapy, schizophrenia, in, (1940) 493
- Hypogonadism
pituitary tumour associated with, (1939) 475
treatment,
testosterone and testosterone propionate, (1941–1942) 384
testosterone propionate, (1940) 525
- Hypoparathyroidism, (1941–2) 322, (1944) 46
cerebral calcification, symmetrical, associated with, (1940) 432
dihydrotachysterol in treatment, (1940) 432
pregnancy, in, (1941–2) 323
vitamin D and A T 10 in, (1940) 589
- Hypopharynx, surgical diseases of, (1943) 309
- Hypophoria, new tests for, (1940) 546
- Hypophysectomy, complete, (1943) 310
- Hypopituitarism
involutorial melancholia and, (1944) 347
pernicious anaemia and, (1944) 129
Simmonds's syndrome, (1944) 45
- Hypopituitary myxoedema, (1943) 286
- Hypoproteinaemia, surgical patients, in, (1940) 352
- Hypoproteinaemia
new-born, in, (1940) 16, 31
treatment,
vitamin K, (1940) 591, (1941–2) 427, (1943) 230
cholic acid, and, (1940) 357
synthetic, (1940) 326, 357
tuberculosis, in, (1943) 63
- Hypopyon in mine workers, (1939) 290
- Hypospadias, surgical treatment, (1940) 576
- Hypotension
aviation, in relation to, (1939) 236
incidence and aetiology, (1941–2) 167
paredrine in treatment of, (1940) 176
post-operative hemiplegia associated with, (1941–1942) 167
postural, (1941–2) 166
causing transient paralysis, (1940) 217
spinal anaesthesia, in, (1940) 176
systolic and diastolic pressures, (1941–2) 167
- Hypothalamic-pituitary syndromes, (1940) 465
- Hypothalamo-hypophyseal complex, (1940) 66
- Hypothalamus
functional localization in, (1940) 65
heat regulation and, (1940) 65
peptic ulcer, role in, (1944) 318
thyroid and, (1940) 66
water metabolism and, (1940) 66
- Hypothyroidism
angina of effort due to, (1944) 46
angina pectoris, in, (1940) 181
carbohydrate tolerance in, (1941–2) 306
migraine, associated with, (1939) 433
myxoedematous, resembling angina, (1939) 215
vitamin D and A T 10 in, (1940) 589
- Hypovitaminosis *See* Deficiency diseases, Vitamins
- Hypoxia, anaesthesia causing, (1943) 120
- Hysteria, hypnosis treatment of, (1939) 378
- Hysterical
dysphagia, (1940) 146
oedema of hand and forearm, (1940) 426
paralysis, soldier, in, (1941–2) 363
stupor,
treatment with cardiazol, (1944) 341
- I
Ichthyosis, (1940) 345
Rud's syndrome, (1939) 379
simplex, (1943) 246
- Icterus gravis neonatorum, (1941–2) 140, (1943) 119
blood transfusion in, (1939) 250
erythroblastosis with, (1941–2) 140
hepatic changes in, (1941–2) 141
vitamin K therapy, (1940) 32; (1941–2) 141
- Idiocy, congenital amaurotic family, (1943) 172
- Idiopathic steatorrhoea, (1941–2) 26
- Ititis, regional. *See also* Crohn's disease
complications of, (1939) 49
- Ileo-gastric syndrome, (1944) 147
- Ileostomy
ulcerative colitis in, (1940) 27, (1944) 20, 183

CUMULATIVE INDEX

Ileum
 carcinoid tumours of, (1943) 253
 obstruction of, (1943) 254
 perforation of, opposite Meckel's diverticulum, (1943) 102
Ileus, (1943) 252 *See also* Intestinal obstruction
 duodenal, (1943) 254
 gall-stone, (1941-2) 125
 paralytic, use of Miller-Abbott tube in, (1941 2) 272
Iliae fossa pain of cervical origin, (1939) 34
Ilium, hydatid cyst involving, (1941-2) 259
Illegitimacy, infant mortality, in relation to, (1939) 38
Immersion foot and hand, (1944) 239
Immunity, (1941-2) 260
 acquired, (1941-2) 260
 active, effect of ultra-violet radiation, (1941-2) 260
 immunization, and, (1939) 379
 enteric fevers, Vi-antigen in, (1939) 380
 vaccines, shock reactions from injections of, (1939) 379
 infections, streptococcal, (1941-2) 261
 passive, (1941 2) 260
 peritoneal, (1944) 320
 poliomyelitis, in, (1944) 39
 practical applications, (1941 2) 260
 tetanus, in, (1944) 383
 yellow fever, in, (1943) 85, 381
Immunization, (1941-2) 260 (1943) 55
 active, recent advances in, (1944) 63
 combined, in tetanus and diphtheria, (1941 2) 260
 diphtheria, in, (1940) 272, (1943) 55, 190
 enteric fevers, in, (1941-2) 261
 infections, acute specific, in, (1939) 16
 infective diseases, in, (1941-2) 69, (1944) 63
 influenza, in, (1943) 5, (1944) 265 7
 measles, in, (1944) 300
 poliomyelitis, in, (1944) 39
 scarlet fever, in, (1941-2) 378, (1943) 329
 tetanus, in, (1940) 552, (1943) 55, (1944) 383
 enteric fever, and, (1941 2) 407
 triple, against diphtheria, whooping-cough and tetanus, (1943) 56
 typhus fever, in, (1943) 5, 56, 84, 371
 epidemic, (1941 2) 416
 whooping-cough, in, (1943) 55, 380, (1944) 408
 yellow fever, in, (1943) 5, 381
Impetigo, (1944) 255
 actiology, (1944) 255
 bacteriology, (1944) 255
 contagious,
 treatment,
 calomel ointment, (1940) 345
 rubber impregnated with 8-hydroxyquinoline, (1940) 346
 Forces, in, (1944) 257
 recent work on, (1944) 257
 sulphonamides, oral administration of, (1943) 246
 treatment, (1941 2) 120, (1944) 256 8
 coffee beans, with, (1939) 381
 general and local, (1944) 256
 iron perchloride, (1944) 256
 sulphonamides, (1944) 256
 ulceron, with, (1939) 381
Impotence
 treatment,
 hormones, with, (1943) 335, (1944) 50
 testosterone propionate, with, (1941-2) 261
Inclusion bodies, multiple carcinoma, in, (1944) 123
Incontinence, stress, (1944) 397
Indian gum, allergic reaction to, (1940) 160
Industrial
 health, during present war, (1940) 9
 medicine, (1944) 259
 bagassosis, (1944) 372
 dermatitis, (1944) 373
 fatigue, (1944) 259
 foundries, health hazards in, (1944) 386
 fur industry, (1944) 260
 hygiene, (1944) 259
 industry, new dangers in, (1944) 388
 lighting, (1944) 259
 mass radiography in, (1944) 68
 oral hygiene, importance of, (1944) 386

Industrial—continued
 medicine -continued
 * prophylactic measures, (1944) 259
 solvents, toxicology of, (1944) 387
 women, health of, (1944) 259
 X-ray injuries, (1944) 388
 psychiatry, (1943) 69
 Workmen's Compensation, (1943) 69
 workers, nutrition of, (1944) 235
Industry *See also* Factory workers
 burns in, (1940) 238
 coronary thrombosis in, (1944) 140
 mass radiography in, (1943) 320
 poisoning in, (1943) 6, 364
 pulmonary tuberculosis in, (1943) 320
 rehabilitation in, (1944) 360
Infant
 anaemia, hypochromic, of, (1943) 116
 arachnoidactyly in a Chinese, (1943) 160
 arteriosclerosis in, (1941-2) 152
 beri-beri in, (1943) 143
 blood transfusion in, (1939) 250
 broncho-pneumonia in, (1941 2) 178
 caloric intake in, (1943) 246
 cardiac enlargement, idiopathic, in, (1943) 233
 diarrhoea in, (1941 2) 208, (1943) 188
 feeding, (1939) 381, (1940) 346, (1941 2) 262, (1944) 260-4
 apple in diet, (1939) 382
 banana in diet, (1939) 382
 dextrin-maltose-dextrose carbohydrate, use of, (1941 2) 262
 digestibility, (1944) 263
 feeding reflexes, (1944) 262
 honey in diet, (1939) 382
 infant mortality, in relation to, (1939) 38
 maternal diet, relation of to lactation, (1941-2) 262
 milk, properties of, (1939) 381
 recent work on, (1944) 263
 requirements of normal and premature infants, (1943) 246
 vitamin C in relation to, (1939) 382
 vitamins in, (1941-2) 49
 histoplasmosis in, (1941 2) 257
 mortality,
 maternal nutrition and, (1944) 22, 142-5
 reduction of, (1939) 37
 myotonia congenita, diagnosis of, (1940) 415
 oestradiol and desoxycorticosterone acetate for, (1941 2) 335
 peptic ulcer in, (1943) 300
 plasma-prothrombin titrations in, (1941-2) 241
 pneumonia in (1941-2) 352
 scurvy in, (1941-2) 379
Infantile
 colitis, associated with, (1940) 249
 dwarfism and, (1943) 197, (1944) 208
 hormone treatment, (1943) 197, 335
 ovarian, (1944) 208
 pterygo-nuchal, (1943) 197
Infant
 cardiac, (1941-2) 249
 coronary thrombosis in, (1940) 185
 atypical, (1944) 141
 rupture of interventricular septum due to, (1941-2) 146
 pulmonary *See* Lung, infarction
 spleen, of, septic, (1940) 541
 testis, of, (1940) 551
Infarction
 myocardial, course and prognosis, (1943) 125
 renal, (1940) 364
Infection
 acute, (1941 2) 62
 aerial contamination, (1944) 41
 aerosols as bactericidal agents, (1943) 53
 air-borne,
 diphtheria, (1941 2) 209
 direct, and, (1943) 54
 carbohydrate metabolism and, (1941-2) 306
 cross, (1941 2) 13, (1943) 51, 248
 eating utensils, contamination of, (1944) 42
 focal, ophthalmology, in, (1944) 367
 head injuries, in, (1943) 9

CUMULATIVE INDEX

Infection—continued

irradiation, ultra-violet, in, (1943) 53, 105
 air in hospitals, of, (1941-2) 130
 oiled floors and oiled linen, (1943) 53
 sources of, (1943) 50, 53
 spread, control of, (1943) 52
 transmission of, (1944) 41
 wounds of. *See* Wounds, infected

Infective

diseases, (1941-2) 4, 62, (1943) 4 *See also* names of particular diseases

acute, (1944) 57
 administrative procedure, (1944) 64
 epidemiological review, (1944) 57
 immunization, active, (1944) 63
 present war, during, (1944) 10
 prophylaxis, (1944) 63
 immunization scheme, (1941) 2 69
 treatment, recent developments in, (1944) 64
 war-time, in, (1944) 57
 fevers, (1939) 74, (1943) 48 *See also* Diphtheria, Infections, Measles, Scarlet Fever, Whooping-cough
 chemotherapy in, (1943) 54
 host, disinfection of, (1943) 52
 immunization, (1943) 52
 infecting agents, (1943) 52
 prophylaxis, specific, (1943) 55
 statistical review, (1943) 48

Influenza, (1939) 383, (1940) 4, (1941) 2 262, (1944) 264-7

aetiology, (1944) 264
 bronchiolitis, acute, in, (1941-2) 263
 buccal spots in, (1941) 2 263
 clinical picture, (1941) 2 263, (1944) 264
 comparison with other virus diseases, (1944) 264
 epidemiological types, (1944) 264
 epidemiology, (1941) 2 262
 immunization (1939) 16, (1944) 265-7
 new filtrable agent, (1939) 383
 present war, during, (1944) 10
 problem, review of, (1944) 266
 prophylaxis, (1944) 265-7
 recent work on, (1944) 58
 swine. *See* Swine influenza
 transmission to animals, (1939) 383
 treatment, (1944) 265
 ineffectiveness of drugs and vaccines, (1944) 264
 preventive, (1944) 265
 vaccination against, (1943) 5
 virus, (1944) 264
 strains, variation of, (1941-2) 262
 viruses of, (1941-2) 3
 war-time, in, (1941-2) 263

Influenzal meningitis, sulphapyridine in, (1940) 404
 Infra-red

photography, chronic hepatitis, in diagnosis of, (1939) 409

rays, burns, in treatment of, (1939) 269

Inguinal

adenitis, lymphopathia venereum causing, (1941) 2 300
 glands, enlarged, in lymphopathia venereum, (1940) 398

Injection

intramuscular, (1944) 16
 pharmacopoeial, (1941-2) 112
 treatment,
 haemorrhoids, of, (1941) 2 375
 hernia, of, (1941-2) 255
 hydrocele, of, (1941-2) 406

Injury, (1939) 383, (1940) 347-53, (1941-2) 263, (1943) 8, 247, (1944) 267-74 *See also* Fractures, Head injuries, Wounds

abdomen, of, (1940) 347, 349
 adherent scars, human oil injections in treatment of, (1939) 386
 alcohol as antiseptic, (1939) 384
 blast, (1943) 251
 celluloid in cranial injuries, (1939) 385
 chest, of, (1940) 349
 crush, (1941-2) 269
 renal failure in, (1943) 249
 rupture of duodenum in, (1943) 250
 treatment of, (1943) 250

Injury—continued

electrical, (1943) 10, 199
 face, of, (1940) 348
 first aid, essentials of, (1944) 271
 gas gangrene prophylaxis, (1939) 385
 head, of, (1940) 348
 crash helmets, use of, (1943) 8, 250
 wound management, (1943) 8
 infection, sources of, (1940) 347
 intrathoracic, (1943) 9, 247
 mercurochrome in pyelonephritis, (1939) 384
 sterilization of oral mucous membrane, (1939) 385

mercury compounds in sterilization of instruments, (1939) 384

metaphen in sterilization of oral mucous membrane, (1939) 384

morphine, administration of, (1944) 271

parachute landings, in, (1939) 383

rehabilitation, (1943) 10

Rideal-Walker test, (1939) 385

treatment,

amniotic membrane, in, (1940) 348
 anaesthetics, local, in oil, (1940) 349
 antiseptic emulsions, (1943) 248
 aponeurotic transplantation, (1940) 348
 aseptic pus, in, (1940) 349
 Cellophane, in, (1940) 349
 closed plaster, in, (1940) 350
 cod-liver oil, in, (1940) 350
 other oils, and, (1943) 248
 electrolysis in Bunyan envelope, (1943) 249
 embryonic extract, in, (1940) 351
 fluids, injection of, (1940) 348
 hypoproteinaemia, (1940) 352
 maggots, in, (1940) 352
 pleural drainage, (1943) 249
 pneumothorax, artificial, in, (1940) 349
 primary suture, in, (1940) 348
 radiotherapy in, (1939) 514
 sodium sulphate, hypertonie, (1940) 351
 sulphanilamide, local, (1940) 351
 surgical, (1943) 10, 247
 tourniquet, new type, (1940) 347
 transparent bandage, (1940) 349
 zinc peroxide, (1940) 349
 war, civilians and, (1944) 343
 wounds, painless closure of, (1939) 385
 sulphanilamide, effect of, on healing of, (1939) 386

zephiran, use of, (1939) 385
 Innominate artery, kinked carotid simulating aneurysm of, (1940) 180

Inquests, fees at, (1941-2) 199

Insanity, puerperal, progesterone treatment, (1944) 352

Insecticide, dermatitis caused by, (1940) 258, 280

Insomnia, (1939) 396

aetiology of, (1939) 386

barbitone hypnotics in, (1939) 19

hypnotic treatment in, (1939) 378

insulin for, (1939) 387

survey of, (1939) 19

Instruments, mercury compounds in sterilization of, (1939) 384

Insulin

acne treated by, (1940) 148

alcohol tolerance, effect on, (1939) 195

allergic reaction to, (1940) 160

alum-precipitated, (1940) 266

alum-insulin substance in blood, (1943) 64

avitaminosis, and, (1940) 265

blood-sugar and respiratory quotient, in relation to, (1939) 301

bone and joint tuberculosis, in, (1940) 226

coma, (1943) 245 *See also* Coma, Diabetes mellitus

crystalline, regular, and zinc-protamine, comparative merits of, (1940) 266

Decurvon pectin-insulin, (1940) 267

diabetes, in, (1939) 303, (1944) 200

mellitus, in, (1940) 265-7 *See also* Diabetes mellitus

insulin-quinine mixture, (1941-2) 207

treated with insoluble preparations of, (1939) 18

CUMULATIVE INDEX

Insulin—continued

- discovery of, (1940) 4, 8-
- dysmenorrhoea, therapy in, (1939) 321
- glucose and, in alcoholism, (1940) 157
- insomnia treated with, (1939) 387
- new preparations, (1943) 33
 - clear protamine zinc, (1943) 34
 - globin (zinc), (1943) 34
 - hexamine, (1943) 34
 - histone zinc, (1943) 34
- oral, (1943) 33
- pancreatic tumours, hypersecretion in, (1943) 245
- pancreatrophic principle, (1940) 452
- plasma potassium, effect on, (1940) 113
- protamine and zinc protamine, (1940) 266
- protamine hexamine, (1940) 267
- pulmonary tuberculosis treated with, (1941-2) 293
- shock, allergy, in, (1939) 201
- shock therapy, (1941-2) 81, (1944) 73
 - asthma, in treatment of, (1939) 232
 - cerebrospinal fluid proteins, effect on, (1941-2) 368
 - economical war-time method, (1941-2) 367
 - intravenous administration, (1941-2) 368
 - Korsakow's syndrome, in, (1940) 497
 - mechanism, (1940) 58
 - mental diseases, in, (1939) 116, (1940) 58
 - psychoses, in, (1939) 498
 - risks, (1944) 73
 - schizophrenia, in, (1939) 116, 503, (1940) 58, 493, (1941-2) 367, (1943) 67; (1944) 348
 - premedication with, (1940) 493
 - spine, compression fracture of, (1941-2) 367
 - technique, (1944) 74
 - suppositories, (1940) 265
 - tuberculosis of bones and joints, in, (1940) 226
 - zinc-globulin, (1940) 267
 - zinc protamine, (1939) 303, (1940) 265, (1941-2) 206
 - allergic dermatitis after, (1943) 187
 - non-diabetic individuals, effects on, (1940) 452
 - soluble, and, combined use of, (1940) 266
- Insurance, life, tuberculosis and, (1940) 94
- Intelligence tests
 - group, Forces in, (1944) 78
 - head injury, in cases of, (1940) 60
 - psychoses, in, (1944) 78
- Interauricular septum, defects of, (1941-2) 247
- Interarterial glomerulo-sclerosis and diabetes mellitus, (1941-2) 152
- Intercostal nerves, temporary elimination of, in pulmonary tuberculosis, (1940) 393
- Intermenstrual pain, (1941-2) 21
- Intermittent claudication, eupaverin for, (1939) 20
- Interstitial keratitis, (1939) 130
- Interventricular septum. *See* Septum
- Intervertebral disks
 - calcification, generalized of, (1943) 137
 - dislocation of, (1941-2) 14
 - disorders of, (1943) 331
 - lesions, radiological diagnosis of, (1943) 350
 - nucleus pulposus of, extrusion of, (1939) 122
 - prolapse and calcification, (1943) 350
 - protrusion of, (1940) 537
 - clinical picture, (1940) 538
 - diagnosis, (1940) 537
 - osteitis deformans, associated with, (1941-2) 396
 - sciatica, as aetiological factor in, (1940) 6
 - X-ray diagnosis, (1940) 538
 - removal, for sciatica, (1944) 365
 - ruptured, diagnosis of, (1943) 350
 - sciatica, relation to, (1940) 516, (1944) 363-6
- Intestinal
 - decompression, (1943) 252
 - obstruction, (1939) 387, (1941-2) 271
 - acute, (1941-2) 271
 - clinical picture, (1941-2) 271
 - diagnosis, (1941-2) 271
 - gall-stones or endoliths causing, (1941-2) 125
 - radiological examination, (1941-2) 271
 - reversed rotation of intestine accompanied by encapsulating peritonitis, (1941-2) 271
 - small intestine, of. mechanical, (1943) 252

Intestinal—continued

- obstruction—continued
 - acute—continued
 - treatment, (1941-2) 272
 - intraperitoneal sulphanilamide, (1941-2) 272
 - Miller-Abbott tube, (1941-2) 272; (1944) 275
 - adhesions causing, (1941-2) 330
 - carcinoid tumours of ileum, (1943) 253
 - closed loop, appendicitis as, (1944) 146
 - congenital
 - bands causing, (1941-2) 272
 - duodenal ileus, (1943) 254
 - obstruction, (1943) 253
 - new-born, in, (1944) 234
 - decompression, treatment by, (1943) 252
 - diagnosis by auscultation, (1943) 102
 - Miller-Abbott tube, use of, (1943) 12, 102, 252
 - duodenal
 - ileus, (1939) 388
 - leiomyosarcoma, (1939) 388
 - hernias causing, (1940) 353
 - intussusception, (1939) 387
 - barium enemas in, (1939) 387
 - jejunum and ileum, of, (1943) 254
 - primary carcinoma, (1943) 254
 - Miller-Abbott tube, use of, (1940) 12
 - nervous system, influence of, (1940) 354
 - small intestine, (1941-2) 272
 - polypoid of, (1939) 388
 - soldiers, in, (1943) 12
 - treatment, (1940) 12
 - vitelline vascular system, remnants of, causing, (1940) 354
 - Wangenstein tube, use of, (1940) 12
 - perforation, foreign bodies causing, (1944) 120*
- Intestine
 - chronic nephritis, lesions in, (1940) 420
 - diseases, vitamin C deficiency and, (1940) 588
 - gas cysts of, (1941-2) 272
 - intubation, in treatment of intestinal obstruction, (1941-2) 272
 - reversed rotation of, (1941-2) 271
 - small,
 - deficiency diseases in relation to, (1940) 5
 - giardial infection, (1941-2) 24
 - leiomyosarcoma, (1944) 275
 - obstruction of, (1941-2) 272, (1944) 275. *See also* Intestinal obstruction
 - congenital, surgical treatment, (1940) 14
 - bands, by, (1941-2) 272
 - X-ray therapy, effect of, on, (1941-2) 372
 - Triboulet's test in diagnosis of tuberculosis of, (1939) 389
 - tuberculosis, (1941-2) 273
 - calcium gluconate in, (1940) 355
 - ulcers, simple of, (1941-2) 193
- Intracranial
 - aneurysms, (1943) 123
 - collections of lipiodol, (1940) 502
 - haemorrhage in new-born, (1940) 16, 32
 - syphilis, (1941-2) 315
 - tumour,
 - erythraemia complicated by, (1944) 231
 - otoneurological diagnosis of, (1939) 94
 - volume, effect of altitude changes on, (1941-2) 160
- Intradiploic epidermoid, (1940) 261
- Intramuscular
 - injections, (1944) 16
 - fluids, of, (1940) 348
 - lipoma, (1941-2) 310
- Intranuclear inclusion bodies in encephalitis epidemica, (1943) 200
- Intra-ocular pressure, high altitudes, at, (1941-2) 160
- Intrasternal introduction of bone marrow, (1941-2) 141
- Intravenous
 - drip arsenotherapy, (1943) 90, 356
 - therapy,
 - bacterial and protein contamination, (1941-2) 337
 - pyrexial reactions, (1941-2) 337
 - transfusion, pyrogen-free water, preparation of, (1940) 356

CUMULATIVE INDEX

Intussusception

- acute, aetiology and clinical picture, (1944) 120
- barium enema in, (1940) 353
- chronic, clinical picture, (1941-2) 126
- diagnosis and treatment, radiological, (1940) 353
- Inulin clearance test, kidney function of, (1940) 118
- Involuntal
 - melancholia,
 - convulsion therapy in, (1941-2) 79
 - endocrine therapy in, (1941-2) 191, 365
 - hypopituitarism and, (1944) 347
 - oestradiol benzoate in treatment, (1940) 488
 - psychoses
 - endocrines in, (1944) 347
- Involuntal-depressive psychoses, convulsive therapy, modified, (1940) 488

Iodine

- acne caused by, (1940) 147
- and potassium iodide mixture, Vincent's angina, in, (1940) 410
- poisoning, (1940) 555
- thyroid gland and, (1940) 314
- Iodism, (1940) 555
- Iodized oil *See* Lipiodol
- Iodobismitol neurosyphilis treated by, (1941-2) 316
- Iodoxy (uroselectan B), (1940) 127
- Ionization
 - cervicitis, in, (1940) 288
 - pelvic iontophoresis, (1941-2) 217
- Iontophoresis
 - chemotherapy by, in ophthalmology, (1944) 220
 - pelvic, (1941-2) 217
 - ringworm treated by, (1943) 217
- Ipecacuanha, relative value as expectorants of potassium iodide and, (1940) 453

Irido-cyclitis

- tuberculous, (1941-2) 420
- uveo-parotitis, (1941-2) 420
- Iritis, ankylosing spondylitis, in, (1941-2) 156
- Iroko wood, dermatitis caused by, (1941-2) 203

Iron

- absorption in body, (1944) 22
- anaemia, in treatment of, (1939) 54, 205
- dosage, (1940) 6
- pregnancy, of, in, (1940) 187
- ankylostoma anaemia treated with, (1940) 187
- deficiency, essential juvenile, (1941-2) 139
- excretion by intestine, (1939) 141
- haemoglobin metabolism, in, (1943) 25
- leukaemia, content of serum in, (1940) 384
- salts, pigmentation caused by, (1940) 235
- therapy in pregnancy, (1939) 220
- trichuriasis treated with ammonium citrate and, (1940) 420
- wholemeal bread as source of, (1943) 213

- 'Iron lung', in treatment of respiratory paralysis, (1940) 6

- Iron perchloride, impetigo treated with tincture of, (1944) 256

Irradiation

- air in hospitals, (1941-2) 130
- necrosis after, (1941-2) 130, (1943) 323 *See also* Radium therapy
- sickness, treatment, (1940) 505

Ischaemia

- degeneration, in relation to, (1939) 15
- limbs, surgical treatment of, (1939) 61
- Isinglass, transfusions of, in haemorrhage, (1941-2) 269

- Itch, cat, (1941-2) 390

- Ito-Reenstierna skin test, (1940) 91

- Ivy, poison, dermatitis caused by, (1941-2) 203

- Ixodid ticks, tick-bite fever transmitted by, (1940) 80

J

- Jaundice, (1939) 389; (1941-2) 273, (1944) 275
 - acholuric, (1944) 133
 - differential diagnosis, (1941-2) 141
 - allergic, (1940) 359
 - allergy, relation to, (1939) 389
 - anaemia, pernicious, associated with, (1940) 168
 - appendicitis, operation for, after, (1941-2) 149
 - arsphenamine causing, (1941-2) 332
 - calculi in right kidney causing, (1943) 255

Jaundice—continued

- catarrhal, (1943) 267. *See also* Hepatitis, infective
- aspiration biopsy of liver in, (1940) 28
- diagnosis, (1940) 359
- hepatitis, acute, and, (1940) 28
- histamine provocation, (1940) 359
- true, evidence for, (1940) 30
- vitamin A absorption, (1940) 359
- choline-esterase index in, (1940) 387
- desensitization treatment, (1939) 389
- diagnosis, (1940) 356, 359
- differential diagnosis by vitamin K test, (1943) 255

- epidemic *See also* Hepatitis, infective
- epidemic catarrhal jaundice as virus disease, (1939) 189

familial

- acholuric, (1944) 133
- non-haemolytic, (1941-2) 141
- galactosuria in, (1940) 359
- glandular fever complicated by, (1943) 222
- haemorrhage, post-operative, (1939) 390
- hepatitis, chronic, with predominant, (1941-2) 289
- hepato-renal disease, (1940) 356
- histamine provocation, (1940) 359
- infections, association with, (1944) 289
- infective, (1940) 358, (1944) 62
 - hepatic, causes of, (1944) 276
- latent, diabetes mellitus, in, (1940) 263
- non-haemolytic, familial, (1941-2) 141
- nuclear, (1941-2) 141
- obstructive,
 - plasma lipids in, (1943) 148
 - renal calculi causing, (1943) 255
 - vitamin K in prevention of haemorrhage during, (1940) 4, 6

- obstructive hepatic, (1940) 357, (1941-2) 273
- hypoproteinaemia, (1940) 357
- hypovitaminosis A and D, (1941-2) 273
- post-operative bleeding, control of, (1940) 357
- post-operative vitamin K deficiency, (1941-2) 273
- pre-operative administration of vitamin K, (1941-2) 273
- prolonged dark-adaptation in, (1941-2) 273
- prothrombin deficiency in, (1941-2) 273
- vitamin K and cholic acid in, (1940) 357
- pneumonia, association with, (1944) 332
- post-arsphenamine, (1944) 35
- post-salvarsan, (1939) 389
- red blood-cells, estimation of diameter of, (1940) 356

- serum, (1944) 35, 62
- spirochaetal (1943) 255 *See also* Spirochaetosis
- icterohaemorrhagica

- spirochaetosis icterohaemorrhagica (Weil's disease), (1939) 390

- conjunctiva in, (1939) 390
- sulphanilamide in presence of, (1940) 359
- therapeutic, in rheumatoid arthritis, (1939) 227
- toxic, (1940) 358
 - causes of, (1944) 276
- treatment, (1940) 13, 357-60
- vitamin K, (1940) 13
- trinitrotoluene causing, (1943) 6
- tropical diseases, complication of, (1944) 276

Jaw

- estimation of age from, (1941-2) 303
- gunshot fracture of, (1944) 18
- median mental sinus, (1940) 412
- oro-maxillary fistulae, (1944) 304
- ulcer, non-malignant, (1941-2) 308

- Jejunocolic fistula, nutritional oedema due to, (1941-2) 318

- Jejuno-ileal insufficiency, chronic, (1941-2) 26

Jejunum

- leiomyosarcoma of, (1941-2) 272
- obstruction of, (1943) 254
- primary carcinoma of, (1941-2) 272, (1943) 254
- sarcoma of, (1941-2) 272
- sprue, in, (1941-2) 27
- Jensen's rat sarcoma, X-ray therapy, (1941-2) 372
- Job's disease, (1943) 300
- 'Jodbasedow', (1940) 314
- Joint pains, caisson disease, in, (1940) 239

CUMULATIVE INDEX

Joints

- arthroplasties, Cellophane in, (1939) 392
- aspiration of, (1940) 200
- atrophy, post-traumatic, (1940) 361
- caisson disease, lesions in, (1940) 239
- degenerative and proliferative changes, (1940) 362
- derangements, traumatic, (1940) 362
- diseases, (1940) 7, 360, (1943) 255, (1944) 276
- disorders, and, (1939) 390, (1941-2) 274
- malignant synoviomias, (1943) 256
- effusions, aspiration of, (1940) 200
- foreign bodies in, (1940) 360, (1943) 256
- hip, osteotomy for osteoarthritis of, (1939) 391
- injuries, (1940) 361
- internal derangements, and, (1939) 392
- cysts of external semilunar cartilage, (1939) 392
- joint measurement, method of, (1939) 392
- manifestations of tuberculous toxæmia, (1940) 567
- osteocondritis dissecans, (1940) 360
- patella, habitual dislocation of, (1939) 392
- pulmonary osteoarthropathy, (1939) 390
- radiography, (1940) 102
- sprains, procaine injections for, (1941-2) 159
- tuberculous, (1941-2) 274
- hip, arthrodesis of, (1939) 391
- knee, surgery of, (1939) 391
- wounds, penetrating, (1940) 361
- Jung, influence of, (1940) 7

K

- Kahn
- test, (1941-2) 103, (1943) 88, 356, 359, (1944) 104
- verification test, (1943) 87, 355, 359

Kala-azar

- aetiology, (1944) 97
- children, in, (1940) 363
- diagnosis, (1940) 362
- diamidines in, (1941-2) 100
- splenic puncture in, (1940) 362
- sternal puncture in, (1940) 362
- survey of, (1939) 147
- transmission by *Phlebotomus argentipes*, (1944) 97
- treatment, (1944) 98
- 4'-diamidinostilbene, (1940) 362, (1941-2) 274
- neostebene, (1943) 256
- synthalin, (1940) 78

- Kapilon, (1940) 131 *See also* Vitamin K
- Kaposi's pigmentary sarcoma, (1943) 347, (1944) 374
- Karaya (Indian) gum, (1940) 160
- Kayser-Fleischer ring, (1943) 241
- Keetley's operation for undescended testis, (1940) 14

Keloid

- aetiology of, (1941-2) 275
- causes, (1944) 277
- operation scars, radiotherapy of, (1943) 256
- treatment, (1944) 277
- Kendall's compound L, (1940) 154
- Kenny treatment of poliomyelitis, (1944) 333
- Keratitis, (1939) 292
- band-shaped, associated with arthritis, (1943) 180
- herpetic, treatment by ether, (1943) 179
- interstitial,
- corneal transplantation in, (1940) 254
- foods, sensitivity to, (1940) 254
- treatment of, (1943) 179
- intravenous injections of ascorbic acid in, (1941-2) 198
- mustard-gas, (1944) 192
- oligoseptic treatment, (1940) 445
- phosphorus causing, (1944) 192
- rosacea, riboflavin therapy, (1940) 254
- trachomatous, neoprontosil instillations in, (1940) 565

- Kerato-conjunctivitis, epidemic, isolation of possible specific agent, (1944) 187

- Keratoconus, vitamin D therapy in, (1939) 293

Keratoderma

- blennorrhagica, (1939) 155
- senile, (1941-2) 191

- Kerato-iritis, beta-rays of radium in treatment, (1940) 579

- Keratomalacia, vitamin A deficiency and, (1941-2) 209

- Keratosis, (1941-2) 394
- blennorrhagica, (1943) 136
- aetiology, (1940) 320
- fever therapy, (1940) 321
- verrucosa, (1940) 345
- follicularis, vitamin A therapy in, (1941-2) 200

- Kernikterus, icterus gravis neonatorum, in, (1941-2) 141

- Ketohydroxyoestrin, prematurity, in, (1940) 482

- Ketonaemia, genito-pituitary adiposity, in, (1940) 152

- Ketosis, diabetes mellitus, in, (1940) 113

- Ketosteroids, neutral, rate of excretion of, (1941-2) 384

- 17-ketosteroids, (1944) 45, 48, 54

- Kettering hyperthermia, general paresis treated by, (1941-2) 105

Kidney

- adenocarcinoma, complicating pregnancy, (1944) 278

- alcoholism affecting, (1939) 196

- alkalosis, in, (1940) 159

- calcification, dissecting aneurysm secondary to, (1941-2) 144

- calcium plaques in, (1941-2) 312

- calculus. *See also* Calculus, renal

- obstructive jaundice due to, (1943) 255

- pathology and composition, (1939) 393

- carbuncle of, surgical treatment, (1943) 259

- cholera, in, (1943) 174

- complications due to sulphathiazole, (1941-2) 343

- congenital abnormalities, (1939) 393, (1940) 363, (1941-2) 275

- metereoele, (1943) 257

- cysts (1939) 394

- hydrotid, surgical treatment of, (1941-2) 258

- unilateral multifocal, (1940) 364

- disease, (1940) 363 71

- advances in knowledge of, (1940) 5

- eclampsia and pre-eclampsia, after, (1940) 17

- hypertension and, (1941-2) 165, (1943) 149

- mercurial diuretics in treatment of, (1940) 5

- ectopia, crossed, (1940) 363

- excision, life after, (1944) 279

- extracts in treatment of renal hypertension, (1941-2) 166

- function, in prostatism, (1943) 313

- tests, (1940) 118

- creatinine clearance, (1940) 118

- inulin clearance, (1940) 118

- one-hour renal condition, (1940) 575

- phenolsulphonethalein (P S P), (1940) 119

- sucrose clearance, (1940) 118

- urea clearance, (1940) 118

- xylose clearance, (1940) 118

- fusion, (1941-2) 275

- glomeruli, intercapillary glomerulosclerosis, (1940) 421

- Goormaghtigh cells, (1944) 161

- hepato-renal syndrome, (1940) 356

- horseshoe, hydronephrosis of, (1943) 258

- hydrocele testis, (1939) 394

- hypernephroma, (1941-2) 277

- metastases simulating aneurysms, (1941-2) 133

- vitilism, and, (1941-2) 133

- impairment of function in crush injuries, (1941-2) 269

- infections, (1940) 364

- injuries, (1941-2) 276

- insufficiency,

- blood transfusion causing, (1941-2) 170

- peritonitis nodosa and, (1944) 150

- prolonged, complicating hyperparathyroidism, (1941-2) 323

- ischaemia of, and hypertension, (1941-2) 2

- lesions,

- blood transfusion causing, (1943) 30

- crush syndrome, in, (1943) 249

- eclampsia, in, (1944) 24

- intravenous hypertonic sucrose solution, after, (1940) 455

- sulphonamide drugs causing, (1940) 457

CUMULATIVE INDEX

Kidney—continued

- lupus erythematosus, in, (1941-2) 299
- malignant disease,
 - familial tendency to, (1940) 366
 - metastatic, (1941-2) 277
- nephrotic syndrome with hypertension in diabetes mellitus, (1941-2) 205
- pain and reflex abdominal pain, (1944) 119
- pelvis, intrarenal, and hypertension, (1944) 161
- permeability, in Addison's disease, (1940) 113
- polycystic disease, (1940) 364
- death from acute uraemia, (1941-2) 275
- post-operative damage, (1941-2) 276
- radiography, (1941-2) 372
- removal, effects of, (1940) 370
- sclerosis, pregnancy toxemia and, (1941-2) 357
- sex hormones, effects of, (1940) 524
- staphylococcal infection of cortex, (1940) 364
- sulphonamides, toxic, effects of, (1944) 328
- suigical diseases, (1939) 393, (1940) 363-71; (1941-2) 275, (1944) 277
- tuberculosis, (1940) 365, (1944) 278
 - bilateral, prognosis in, (1943) 259
 - pyuria, sterile, in, (1940) 365
 - spontaneous healing in, (1943) 259
 - treatment, (1943) 260
 - tubercle bacilli in urine, (1940) 365, (1944) 278
- tubules, concretions in, sulphathiazole causing, (1940) 461
- tumours, (1940) 365, (1941-2) 277, (1944) 278
 - angioma in papilla, (1943) 229
 - diagnosis, (1941-2) 277
 - familial tendency, (1940) 366
 - fever as initial symptom, (1941-2) 277
 - hypertension associated with, (1939) 393
 - metastatic, (1941-2) 277
 - neurofibromas, non-malignant, (1943) 260
- Wilms' embryoma, (1939) 393, (1940) 365, (1943) 260
- xanthine calculi, (1939) 393
- X-ray examination, (1944) 357
- Kleine-Levin syndrome, (1943) 318
- klotogen, (1940) 131 *See also* Vitamin K
- knee
 - chondritis, (1940) 361
 - derangements,
 - internal, (1940) 361
 - traumatic, (1940) 362
 - granuloma, traumatic, (1941-2) 274
 - injuries, athletics causing, (1940) 205
 - joint, surgical approach to, (1940) 275
 - menisci, removal of, (1940) 361
 - semilunar cartilages, radiography, (1940) 102
 - synovial membrane, glomus tumour of, (1941-2) 393
 - synovioma, malignant, (1941-2) 274
 - tuberculosis of, (1939) 391
- Knox cube test, (1940) 61
- Koch-Weeks' bacillus, (1940) 252
- Kohs-Block test, (1940) 60
- Kolmer test, for syphilis, modified, (1940) 547
- Kondolón's operation, (1943) 275
- Korsakow's syndrome, (1939) 196, 506, (1941-2) 369
 - insulin-shock therapy, (1940) 497
 - vitamin-B₁ therapy, (1940) 497
- Kraurosis
 - treatment, (1944) 27
 - synthetic oestrogens in, (1939) 35
 - vulvae, oestrogenic treatment, (1940) 593
- Kretschmer's classification, types of personality, relation to menstrual history, (1940) 339
- Kymography, (1940) 101
 - aortic aneurysm, of, (1939) 213
 - clinical evaluation of, (1943) 321

L

- Laboratories, public health, (1944) 5
- Labour, (1939) 394, (1941-2) 278, (1944) 279-82
 - acetylcholine, action of, (1940) 371
 - amniotic fluid causing pulmonary complications, (1943) 261

Labour—continued

- anaesthesia and analgesia, (1939) 396, (1940) 375; (1941-2) 280, (1943) 261, (1944) 281
 - caudal, (1943) 18
 - continuous, (1944) 281
 - evipan soluble, (1941-2) 280
 - per rectum, (1940) 375
 - foetal asphyxia, (1940) 19
 - paraldehyde analgesia with perineal anaesthesia, (1941-2) 280
 - pentothal acid, (1940) 375
 - antipyrine in, (1939) 397
 - aspiration pneumonitis following, (1940) 235
 - blood loss during, (1944) 23
 - blood transfusion in *See* Blood transfusion, Rhesus factor
 - bombing, effect of, on, (1941-2) 19
 - breech presentation, aetiology of, (1940) 373
 - Caesarean section,
 - complications, (1939) 396
 - scar, healing of, in, (1939) 395
 - cervix, role of, (1940) 372
 - complications of third stage, (1944) 279
 - course of, (1941-2) 278
 - delayed, (1941-2) 279
 - deliveries, incidence of day and night, (1940) 371
 - diabetes and, (1944) 201
 - diet, salt-poor, (1940) 371
 - evisceration and embryotomy, (1941-2) 279
 - factors in, (1940) 372, (1941-2) 278
 - foetal anaemia due to anaesthetics, (1939) 396
 - hydatid cyst obstructing, (1939) 394
 - hypophyseal necrosis, acute, following, (1940) 465
 - induction, (1940) 374, (1941-2) 279
 - alkalinization and pituitary extract, (1941-2) 279
 - disproportion, in, (1944) 280
 - ergot, with, (1940) 374
 - high puncture of membranes, (1941-2) 279
 - oestrogens, with, (1940) 374
 - posterior pituitary extract, with, (1939) 395, (1941-2) 16, 279
 - rupture of membranes, (1940) 374
 - uroselectan B, with, (1941-2) 19
 - labial and paravaginal haematoma following, (1940) 593
 - membranes, rupture of, (1940) 372, 374
 - narcosis in, foetal asphyxia and, (1940) 19
 - normal, (1941-2) 278
 - phenomena of, (1940) 371
 - obstetric shock, acacia in, (1939) 395
 - obstructed,
 - evisceration and embryotomy, (1941-2) 279
 - failure of dilatation of os, (1941-2) 279
 - foetal ascites causing, (1941-2) 279
 - obstruction to,
 - cervix, in, (1941-2) 279
 - dermoid cyst of vagina, (1940) 373
 - occipito-posterior position, mechanism and treatment of, (1944) 24
 - oestrogenic therapy, (1940) 374
 - onset, causes of, (1940) 371
 - oxytocic substance and pituitrin, (1941-2) 278
 - operative and manipulative procedures, (1940) 374, (1941-2) 279, (1944) 280
 - pains, (1940) 371
 - relief of, by raspberry leaves, (1941-2) 20
 - paraldehyde by intramuscular injection in (1943) 261
 - pentothal and thioethamyl in, (1939) 397
 - pituitary extract in, (1939) 395
 - premature, corpus luteum extracts in prevention of, (1943) 333
 - presacral neurectomy, after, (1940) 546
 - primigravidae, elderly, complications in, (1944) 298
 - prolapse of cord, (1941-2) 278
 - pulmonary embolism and, (1944) 280
 - radiology, (1941-2) 280
 - sedatives in, (1941-2) 280
 - stages of, (1940) 371
 - thrombosis and embolism complicating, (1944) 280
 - uterine contractions, effect of stilboestrol, (1940) 372
 - uterus, inversion of, (1940) 373

CUMULATIVE INDEX

Labour—continued

- vitamin K therapy in, (1941-2) 428
- X-ray examination in, (1941-2) 280
- placental implantations, (1941-2) 280
- soft tissue radiography, (1941-2) 280
- visualization of placenta, (1941-2) 280
- Labyrinth, aviators in, (1940) 205
- Labyrinthectomy, labyrinthine vertigo, for, (1940) 583

Lacrimal

- apparatus,
 - concretions, in actinomycosis, (1940) 149
 - diseases, (1939) 397; (1941-2) 281
 - dacryocystitis, chronic, treatment of, (1939) 397
 - dacryocystorrhinostomy, (1939) 398
 - plasmacytoma, (1939) 397
- glands,
 - Boeck's sarcoid of, (1941-2) 281
 - tumours, (1941-2) 281

Lactation

- cystine, glycine and glutamic acid, effect of, (1941-2) 262
- diabetes and, (1944) 201
- draught reflex, (1944) 262
- excretion of mandelic acid, (1941-2) 262
- hormonal control of, (1943) 332, (1944) 52
- inhibition,
 - male sex hormone, by, (1943) 335
 - stilboestrol, by, (1941-2) 262
 - testosterone propionate, by, (1940) 500
- mastitis of, (1940) 231
- mechanism of, (1944) 260
- oestrogens, effect of, (1941-2) 383
- prenatal diet, effect of, (1944) 261
- prolactin, effect of, (1940) 132, 346
- quantity of milk secreted, (1944) 260
- recent work on, (1944) 263
- relation of maternal diet to, (1941-2) 262
- stilboestrol, effect of, (1940) 132

- Lactal obstruction, sprue syndrome, and, (1941-2) 28

Lactoflavin See Vitamin B₆

Lactogenic hormone, (1943) 332

- Laevulose tolerance test, liver function, of, (1940) 116

Lambia intestinalis, (1941-2) 24 See also Giardia intestinalis

Lamblasis, (1941-2) 24 See also Giardiasis

- Laminectomy, sciatica, for, (1944) 364
- Lanatoside C, effect on heart, (1941-2) 337
- Landy's paralysis, vitamin B₁ treatment, (1939) 398
- Lenticular nucleus, functions of, (1941-2) 90
- Larocain in ulcerative colitis, (1939) 287
- Larva migrans, treatment, (1941-2) 310
- Laryngeal neuralgia, superior, (1941-2) 314
- Laryngitis
 - acute,
 - helium-oxygen inhalation in, (1941-2) 281
 - obstructive, surgical treatment, (1944) 282

Laryngocele, pseudo-, (1941-2) 311

Laryngofissure, (1943) 263

Laryngology, (1941-2) 52

- Laryngo-tracheobronchitis, chemotherapy in, (1941-2) 281

Larynx

- anterior commissure tendon, (1943) 263
- Boeck's sarcoidosis, (1941-2) 281
- cancer, teleradium therapy, (1944) 283
- cysts, congenital, (1940) 375
- diseases, (1939) 398, (1941-2) 281; (1944) 282-4
- laryngectomy, prognosis of, (1939) 399
- laryngocele, (1939) 399
- malignant, treatment of, (1939) 90
- tracheotomy, sudden death after, (1939) 398
- tuberculosis, ionization in, (1939) 399
- malignant growths, anaesthesia for, (1941-2) 282
- teleradium therapy, (1944) 283
- papilloma, oestrogenic therapy, (1940) 376
- paralysis, (1944) 283
- tumours, (1940) 375, (1941-2) 281
- benign, (1943) 40, 262
- classification, (1943) 40
- amyloid, (1943) 41, 262
- angioma, (1943) 40

Larynx—continued

tumours—continued

benign—continued

classification—continued

- chondroma, (1943) 41
- cyst, (1943) 41
- fibroma, (1943) 40
- leucoplakia, (1943) 42
- lipoma, (1943) 41
- myxoma, (1943) 41
- neurofibroma, (1943) 40
- papilloma, (1943) 42
- rhabdomyoma, (1943) 41
- xanthoma, (1943) 42
- treatment,
 - irradiation, (1943) 43
 - oestrogen, (1943) 43
 - surgical, (1943) 42
- malignant, (1943) 262
- children, in, (1943) 263
- treatment,
 - surgical, (1943) 262
 - X-ray, (1943) 262
- teleradium therapy, (1944) 283

Lateral

- geniculate body, (1943) 73
- sclerosis, amyotrophic, vitamin E therapy, (1941-2) 307
- sinus thrombosis, treatment by sulphanilamide, (1943) 362

Lathyrism, (1940) 376

Laughlin test, syphilis, for, (1940) 210

Laurence-Moon-Biedl syndrome

- Jorne fruste*, (1941-2) 351
- incomplete form of, (1941-2) 162
- polydactyly and mental deficiency, without, (1941-2) 351

Lazarine leprosy, (1943) 264

Lead

- blood, content in normal, (1940) 377
- cancer of lung, role in production of, (1944) 294
- encephalopathy, (1943) 263
- inhalation, encephalopathy from, (1944) 387
- poisoning, (1939) 400, (1940) 376-8, (1941-2) 282, (1943) 263
- aetiology, (1940) 376, (1941-2) 282
- bismuth therapy causing, (1940) 376
- bones in, (1940) 377
- bullets lodged in tissues causing, (1941-2) 282
- central nervous system in, (1941-2) 282
- children, in, (1940) 377
- clinical picture, (1941-2) 282
- diagnosis, (1939) 400, (1940) 377, (1941-2) 282
- encephalopathy,
 - bone changes in, (1940) 377
 - cerebral tumour, simulating, (1941-2) 282
 - children, in, (1941-2) 282
 - lead inhalation, from, (1944) 387
 - magnesium sulphate treatment, (1939) 400
 - parathormone treatment, (1939) 400
 - printers, in, (1941-2) 282
 - treatment, (1940) 378
 - apple therapy, (1940) 378
 - sodium citrate solution, (1944) 284
 - vitamin C, (1940) 378
- renal calculus containing, (1941-2) 276
- urine, detection in, (1939) 400, (1944) 397
- Lecithin, disseminated sclerosis, in, (1940) 278
- Lederer's anaemia, (1941-2) 140. See also Anaemia, haemolytic, Lederer's

Leg

- diabetes mellitus, lesions in, (1940) 263
- enlargement of, chronic, (1943) 293
- oedema, bilateral, of, (1941-2) 318
- persistent, (1941-2) 318
- ulceration, chronic, skin grafting in, (1944) 39

Leiomyoma

- gastro-intestinal tract, of, (1943) 370
- uterine, mitotic activity in, (1944) 398

Leiomyosarcoma

- duodenum, of, (1940) 355
- heart, of, (1943) 235
- inferior vena cava, of, (1941-2) 422
- jejunum, of, (1941-2) 272
- small intestine, of, (1944) 275

CUMULATIVE INDEX

- Leishmania donovani*, demonstration by sternal puncture, (1940) 362
- Leishmaniasis, cutaneous, (1939) 401; (1940) 378, (1943) 284
- oriental sore, fuchsin paint treatment of, (1939) 401
- trypanosomicides in, (1940) 136
- Lempert's operation for otosclerosis, (1939) 87
- Lenses
- eye injuries from broken, (1940) 253
- lacquered, use in strabismus, (1941-2) 402
- Lenticular changes, following ulceration of cornea, (1944) 192
- Leontiasis ossea, ophthalmological complications, (1940) 225
- Lepromin test, (1944) 284
- Leprosy, (1939) 401; (1941-2) 283
- aetiology, (1940) 379
- alimentary canal, transmission through, (1940) 380
- bacteriology, (1939) 401
- clinical picture, (1939) 402
- cobra venom in treatment, (1939) 402
- diagnosis, (1940) 381
- leprolin test, (1939) 402
- lepromin test, (1944) 284
- differential diagnosis, tumour-like tuberculosis, (1943) 264
- geographical distribution, (1940) 380; (1941-2) 283
- Great Britain, in, (1941-2) 283
- heredity, (1940) 379
- history, (1940) 379
- immunity, (1940) 379
- Lazarine, (1943) 264
- lipomatosis associated with, (1939) 402
- mixed types, (1941-2) 283
- nerve involvement, incidence of, (1943) 264
- paronychia, painless, in, (1939) 441
- pathology and bacteriology, (1941-2) 283
- Portugal, in, (1940) 379
- potassium iodide test, (1940) 381
- prognosis, sedimentation rate as guide to, (1939) 402
- resistance, (1940) 379
- skin lesions, (1940) 380, (1943) 264
- treatment, (1941-2) 283
- basic principles, (1941-2) 283
- blood transfusion, (1941-2) 283
- diphtheria antitoxin and toxoid, (1940) 381
- diphtheria formal toxoid, (1941-2) 284
- Grasset's tubercle endotoxoid, (1941-2) 284
- tuberculoïd, (1941-2) 283
- types, (1944) 284
- ulceration in, (1941-2) 284
- Leptazol, (1940) 127 *See also* Cardiazol
- cardiographic changes due to, (1941-2) 337
- convulsion therapy,
- complications, (1940) 58
- fractures complicating, (1940) 59
- technique, (1940) 58
- depressive states treated with, (1943) 317
- effects of, (1940) 56
- psychomotor efficiency, effect on, (1941-2) 337
- shock therapy, (1943) 66
- bilateral fracture of femoral neck caused by, (1941-2) 366
- cardiovascular patients, in, (1941-2) 367
- compulsion neurosis, in, (1941-2) 364
- effect on cerebrospinal fluid proteins, (1941-2) 368
- fractures of spine caused by, (1941-2) 366
- homosexuality and lesbianism, in, (1941-2) 385
- memory defects following, (1941-2) 367
- results of, (1941-2) 367
- sub-convulsant doses, (1941-2) 365
- affective psychoses, in, (1941-2) 365
- Leptomeningitis
- acute post-operative aseptic, (1943) 279
- Pfeiffer's bacillus causing, (1943) 279
- Leptospira *icterohaemorrhagiae*, serological test, (1940) 358
- Leptospiiral infection, occupational hazard, as, (1943) 255
- Lesbianism, leptazol therapy, (1941-2) 385
- Leucocyte count in pyogenic infections, (1939) 221
- Leucocytes
- interaction of fibroblasts and sarcoma cells with, (1940) 569
- supravital staining of, (1941-2) 7
- Leucocytosis
- adrenaline producing, (1940) 447
- periarteritis nodosa, in, (1939) 224
- psychopathic personality, in, (1943) 315
- Leucoplakia, (1941-2) 394
- buccal, hormone therapy in, (1944) 53
- larynx, of, (1943) 42
- tongue, of, (1940) 410
- treatment, oestrogens, (1944) 27
- synthetic, (1939) 35
- vulvae,
- mercury sulphide tattoo for, (1941-2) 430
- oestrogen treatment of, (1944) 27
- Leucorrhoea
- monilial vaginitis and, (1941-2) 284
- other non-haemorrhagic discharges, and, (1939) 403
- differential diagnosis, (1939) 403
- Trichomonas vaginalis* vulvo-vaginitis, (1939) 403
- arsenic (pentavalent) in, (1939) 403
- silver picrate in, (1939) 403
- pregnancy, in, (1940) 19
- Leucotomy
- effects of, (1944) 72
- frontal,
- mental disorders, treatment of, in, (1941-2) 81, (1943) 67, 316
- technique, (1941-2) 82
- limited scope of treatment, (1944) 72
- mental diseases treated by, (1944) 72
- technique, (1944) 72
- Leukaemia, (1939) 404, (1941-2) 285, (1944) 285
- acute, bone marrow injections in, (1939) 404
- adrenaline injection in diagnosis, (1939) 405
- aetiology, (1939) 404
- aleukaemic, (1940) 382
- lymphatic, (1944) 285
- myeloid, subacute, (1941-2) 286
- sternal puncture in diagnosis of, (1940) 32
- Vincent's angina, associated with, (1940) 383
- atypical manifestations, (1940) 383
- children,
- bone changes in, (1940) 384
- eosinophil in, (1943) 265
- chronic,
- achlorhydria and leukaemia in, (1939) 405
- myeloid, (1941-2) 285
- erythroblastic, (1943) 265
- infections, susceptibility to, (1939) 405
- leukaemoid reactions and, (1941-2) 285
- lymphocytic,
- chronic, (1944) 285
- sternal puncture in, (1940) 383
- sulphapyridine in, (1941-2) 286
- monocytic,
- acute, (1941-2) 286
- chronic,
- aetiology, (1944) 285
- clinical picture, (1944) 285
- myelocytic, (1941-2) 285
- chloroma and, (1941-2) 285
- chronic, (1941-2) 285; (1943) 265
- clinical picture, (1941-2) 285
- leukaemoid reactions and, (1941-2) 285
- morbid anatomy, (1944) 285
- myeloid, (1940) 382
- subacute aleukaemic, (1941-2) 286
- tuberculosis, miliary, associated with, (1940) 382
- phosphorus, radio-active, effects of, (1943) 265
- retinal changes in diagnosis, (1939) 404
- serum, iron content of, (1940) 384
- skeletal symptoms in, (1941-2) 286
- spleen in, (1944) 285
- sternal puncture in, (1939) 247
- subacute aleukaemic myeloid, (1941-2) 286
- X-ray therapy in, (1940) 6
- 'spray' technique, (1941-2) 285
- uraemia after, (1940) 384
- Leukaemoid reaction, (1941-2) 285
- erythraemia, in, (1944) 231

CUMULATIVE INDEX

- Levinson's test, meningitis, tuberculous, in, (1940) 405
 Libman-Sacks syndrome, (1943) 348
 Lice, (1941-2) 391
 control of, (1943) 85
 temperatures lethal to, (1940) 531
 Lichen, (1939) 405
 amyloidosis, (1939) 405
 obtus, (1940) 345
 planus, linear and zosteriform types distinguished, (1939) 405, (1941-2) 286
 aetiology, (1941-2) 286, (1944) 286
 bladder, of, (1940) 207
 clinical picture, (1940) 385
 endocrine factors, (1944) 286
 nail-bed, involving, (1941-2) 287
 treatment by vitamin B, (1941-2) 287
 Ligamentum flavum
 hypertrophy of, (1940) 540
 thickening of, causing sciatica, (1940) 515
 Ligature material, (1944) 15
 Lighting
 industrial, (1944) 259
 prophylaxis of miner's nystagmus by stronger, (1944) 313
 Light sense apparatus, Livingston's, (1941-2) 31
 Limb
 phantom, (1943) 76
 prolonged compression of, (1941-2) 269
 Limbal tumours, (1941-2) 196
 Limbus, carcinoma, primary, of, (1940) 252
 Lindau's disease, (1943) 127
 X-ray therapy, (1940) 385
 Linen, oiled, and control of infection, (1943) 53
 Lipid
 analysis of spleen in Gaucher's disease, (1943) 265
 pneumonia, (1941-2) 177, (1943) 166, 310
 iodized oil, due to, (1944) 331
 Lipids, plasma, in obstructive jaundice and hepatic disease, (1943) 148
 Lipiodol
 bronchiectasis, injections in, (1939) 266
 intervertebral disk lesions, use in, (1944) 364
 intracranial collections of, (1940) 502
 lipid pneumonia due to, (1944) 331
 myelography, in, (1941-2) 371
 persistence in lungs after bronchography, (1943) 322
 pulmonary collapse after injection of, (1944) 66
 radiography of maxillary antrum, (1941-2) 127
 relative merits of oxygen and, (1940) 538
 sterility treated by injection of, (1940) 299
 Lipocae, (1940) 430
 diabetes, complications of, treated with, (1943) 35
 erythraemia treated with, (1941-2) 225
 Lipodystrophia progressiva, xanthoma diabeticorum with, (1940) 263
 Lipoedema, (1940) 427
 Lipoid granulomatosis *See* Schuller-Christian syndrome and Lipoidoses, Schuller-Christian syndrome
 Lipoidoses, (1939) 406, (1941-2) 287
 acute idiopathic cholesterol granulomatosis, (1943) 266
 differential diagnosis, (1941-2) 287
 Gaucher's disease, (1941-2) 287
 aetiology of, (1939) 406
 lipid analysis of spleen in, (1943) 265
 lipophagic granulomatosis of enteric tract, (1943) 266
 Schuller-Christian syndrome, (1941-2) 287
 clinical picture, (1939) 406
 xanthomatous biliary cirrhosis, (1941-2) 287
 Lipoma
 diaphragm, of, (1940) 268
 intramuscular, (1941-2) 310
 intrathoracic, (1944) 295
 larynx, of, (1943) 41
 soleus muscle, in, (1941-2) 310
 Lipophagic granulomatosis of enteric tract, (1943) 266
 Liposarcoma, (1944) 393
 Lipotropic substances, psoriasis treated with, (1944) 338
 Lip-reading, (1939) 107
 Lips
 cancer, prognosis, (1940) 241
 carcinoma of, (1943) 281
 herpes, treated with spiritus vini rectificatus, (1941-2) 256
 hypertrophy, in lymphopathia venereum, (1940) 398
 irritation due to lipstick, (1941-2) 203
 syphiloma, diffuse hypertrophic, (1940) 398
 Lipstick
 cheilitis, (1941-2) 203
 dermatitis due to, (1943) 183
 Liquid paraffin, disinfection of hospital equipment by, (1941-2) 185
 Listerella organisms, glandular fever, relation to, (1941-2) 235
 Little's disease
 aetiology of, (1939) 274
 treatment by β -erythroidine hydrochloride, (1941-1942) 332
 Liver
 amoebic abscess, pleurisy and, (1940) 167
 arsenical treatment of syphilis, effect on, (1940) 549
 ascorbic acid, influence of, (1940) 587
 aspiration biopsy of, (1940) 28
 atrophy, acute yellow, chlorinated naphthalene causing, (1944) 387
 blood, circulation of, in, (1941-2) 288
 carcinoma,
 aetiology, (1944) 290
 intrahepatic gall-stones and, (1944) 290
 primary, (1941-2) 289
 cyst, congenital, of round ligament of, (1940) 388
 disease, (1940) 6, 385-8 (1941-2) 288, (1944) 286-290
 amines, toxic, and, (1940) 54
 chronic venous engorgement, (1939) 408
 morbid anatomy, (1939) 408
 cirrhosis,
 abdominal venous thrill, (1941-2) 288
 aetiology, (1940) 387
 alcoholic, and coproporphyrinuria, (1944) 245
 alcoholism cause of, (1939) 196
 anaemia, pernicious, associated with, (1943) 268
 ascites, and, associated with hernia, (1941-2) 255
 children, in, (1940) 387
 diabetes in children with enlargement of, (1939) 307
 diet,
 and vitamin B complex, in, (1943) 268
 deficient, causing, (1940) 387
 experimental, (1940) 387
 Hanot's unilobular, (1941-2) 289
 hepato-lenticular degeneration, in, (1943) 242
 high fat dietary producing, (1944) 290
 infantile hepatic, (1939) 410
 types, (1939) 410
 multiple neuritis, relation to, (1941-2) 289
 pre-cirrhotic hepatosis in alcoholism, (1941-1942) 135
 vitamin deficiency and, (1943) 268
 hepatitis, acute and subacute, (1939) 408
 acute necrosis of liver in new-born, (1939) 409
 angioma associated with, (1939) 218
 toxic hepatitis, (1939) 408
 hepatitis, chronic,
 aetiology, alcoholism in, (1939) 409
 diagnosis, infra-red photography in, (1939) 409
 obstructive biliary cirrhosis, (1939) 410
 vitamin A in blood in diagnosis and prognosis, (1939) 410
 hepatitis, infective, (1943) 267
 hepato-renal, (1940) 357
 syndrome, (1940) 356
 plasma
 lipids in, (1943) 148
 prothrombin in, (1940) 117
 enlargement,
 diabetes in children and, (1943) 35
 diabetes mellitus, in, (1940) 263

CUMULATIVE INDEX

Liver—continued

- extract,
 - anaemia, in, (1939) 54
 - pernicious, (1939) 203
- capacity to store, (1940) 170
- neuralgia, trigeminal, with vitamin B₁, in, (1940) 423
- seborrhoeic dermatoses, in, (1944) 367
- sprue, in, (1939) 149
- function tests, (1939) 406, (1941-2) 4, 288, (1944) 286-9
 - bilirubin excretion, (1940) 116
 - bromsulphalein, serial, (1944) 288
 - cephalin-cholesterol flocculation test, (1944) 288
 - colloidal gold reaction, (1940) 386
 - comparative review, (1941-2) 288
 - evaluation of various, (1939) 408, (1943) 267
 - fructose-tolerance, (1940) 116
 - galactose-tolerance, (1940) 385
 - glucuronic acid excretion, (1940) 117
 - hippuric acid, (1939) 407, (1940) 116, 386, (1944) 288
 - surgical prognosis, use in, (1944) 287
 - intrahepatic circulation of blood, (1941-2) 288
 - laevulose-tolerance, (1940) 116
 - modification, (1939) 406
 - liver and plasma prothrombin, (1939) 407
 - new galactose-tolerance, (1943) 267
 - old age, in, (1944) 286
 - phenolphthalein, (1941 2) 288
 - present-day value of, (1944) 288
 - prothrombin, (1940) 386, (1944) 288
 - quartz-rod transillumination, (1941-2) 288
 - scarlet fever, in, (1940) 513
 - scope and significance, (1944) 286
 - sensitivity and reliability, (1944) 286
 - serum cholinesterase, (1940) 387, (1944) 287
 - sodium lactate, intravenous dextrorotary, (1944) 287
 - Takata's flocculation, (1939) 407
 - Takata-Ara reaction, (1940) 386
 - vitamin K, prothrombin response to, (1944) 288
- histopathological changes in burns, (1941-2) 178
- necrosis, sulphanilamide as possible cause, (1941-1942) 343
- partial removal, effects of colchicine after, (1941-1942) 334
- phenolphthalein, effect of, (1941 2) 288
- prothrombin and, (1940) 117
- rupture, with subsequent 'sequestum', (1941 2) 263
- sex hormones, effect of, on, (1941-2) 381
- stilboestrol, alleged toxic action of, (1941-2) 383
- testosterone and methyl testosterone, inactivating effect on, (1944) 369
- therapy,
 - coeliac disease, in, (1939) 282
 - colitis, in, (1939) 286
 - pink disease, in, (1944) 330
 - tropical megalocytic anaemia, in, (1939) 204
- tumours, (1940) 388, (1941-2) 289
 - malignant, (1944) 290
 - morbid anatomy, (1941 2) 289
 - racial incidence, (1941-2) 289
- Livido reticularis, (1941-2) 224
- Livingston's
 - angular depth perception apparatus, (1941-2) 31
 - light sense apparatus, (1941-2) 31
 - rotating stereogram, (1941-2) 31
- Lobectomy
 - bronchiectasis, in, (1939) 265
 - frontal, (1940) 71, 228
 - bilateral, (1940) 72
 - mental changes resulting from, (1940) 71
- Lobotomy, pre-frontal, in treatment of mental disease, (1941-2) 365
- Localization by vision, loss of power of, (1943) 76
- Löffler's syndrome, (1941-2) 157
- Longevity
 - rules for, (1944) 367
 - sex and profession as factors, (1941-2) 379
- Looser's zones, (1941-2) 171
- Louise, (1941-2) 391
- Low-voltage varying currents, used for shock therapy in mental disease, (1941-2) 218

Lugol's solution, parotitis, in, (1940) 434

Lumbago, (1941-2) 161; (1943) 142 *See also* Back-ache

Lumbar

- puncture,
 - asthma, in, (1939) 233
 - concussion and compression, in, (1939) 289
 - delirium tremens, in, (1939) 195
 - sources of contamination in, (1943) 173
- sympathectomy for ischaemia, (1939) 61
- sympathetic, novocain infiltration of, in phlebitis, (1940) 582

Lumbo-sacral anomalies, (1943) 142

Lung

- abscess, (1941-2) 290
 - acute putrid, (1941-2) 76
 - aetiology, (1940) 389
 - classification, (1941-2) 290
 - pathology and morbid anatomy, (1941 2) 290
 - treatment, (1941-2) 290
 - bronchoscopic, (1941-2) 290
 - sulphapyridine, (1941-2) 290
- agenesis, (1944) 234
- anatomy, (1944) 66
- atelectasis *See* Atelectasis
- blast injuries, (1941-2) 297, (1943) 271, (1944) 273
 - See also* Blast injuries
 - clinical picture, (1941 2) 297
 - experimental investigation, (1941-2) 298
 - phrenico-costal sinus pneumonia, (1941-2) 298
 - results of air-raids, (1941 2) 297
- carcinoma, (1941-2) 294, (1943) 60, 270, (1944) 69
 - aetiology, (1944) 294
 - bronchogenic, atypical, (1943) 270
 - bronchoscopy in, (1943) 270
 - cardiac
 - infiltration, (1944) 293
 - metastases, (1941-2) 294
 - incidence, (1944) 294
 - lead as aetiological factor, (1944) 294
 - pneumectomy, total, for, (1944) 294
 - primary, (1941-2) 294
 - 'sulcus tumour', (1941-2) 294
- collapse, (1940) 388
 - after injection of iodized oil, (1944) 66
 - bronchiectasis and, (1944) 67
- diseases. *See* Lung diseases, *infra*
- emphysema, interstitial, (1939) 327
- erythraemia, in, (1940) 297
- fibrosis,
 - diagnosis of, (1941-2) 294
 - scleroderma and, in Raynaud's phenomenon, (1941-2) 375
- histoplasmosis of, (1943) 243
- infarction, pneumothorax due to, (1941-2) 290
- injury, blast causing, (1944) 273
- oedema of, associated with menstruation, (1941 2) 318
- persistence of lipiodol in, after bronchography, (1943) 322
- post-operative complications, (1939) 417, (1940) 108, 394, (1941-2) 295
 - anaesthetic, influence of, (1940) 108
 - atelectasis, (1940) 388
 - bronchoscopy in, (1940) 388
 - carbon dioxide as stimulant, (1940) 109
 - embolism, (1939) 417
 - pulmonary, (1939) 419, (1940) 394, (1941-2) 295
 - diagnosis, (1941-2) 296
 - hepatic therapy, (1941-2) 296
 - incidence and occurrence, (1941 2) 295
 - multiple chest-lead cardiograms, (1941-2) 296
 - operative prevention, (1941 2) 296
 - predisposing conditions, (1941 2) 295
 - thrombophlebitis and, (1941-2) 296
 - treatment, (1941-2) 296
- ether, (1940) 108
- thrombosis, (1940) 395
- tuberculosis,
 - extension of, (1941-2) 292
 - radiological examination of, (1939) 417

CUMULATIVE INDEX

Lung—continued

- tularaemia, in, (1943) 369
- tumours, (1940) 394, (1941-2) 294. *See also infra*
 - malignant (1941-2) 294; (1943) 270, (1944) 293-295
 - non-malignant, (1941-2) 294, (1944) 295
 - bronchial adenoma, (1943) 270
 - primary, anoxia and, (1940) 240
- treatment,
 - pneumonecctomy, (1944) 294
 - surgical, (1944) 294
- Lung diseases, (1940) 388-95, (1941-2) 71, 290; (1943) 58, 269, (1944) 66, 290-6
 - abscess and gangrene, (1939) 410
 - clinical picture, (1939) 410
 - acute interstitial pneumonitis, (1939) 418
 - clinical picture, (1939) 418
 - congenital cystic disease, (1939) 418
 - aetiology, (1939) 418
 - complications and diagnosis, (1939) 419
 - morbid anatomy, (1939) 419
 - treatment, surgical, (1939) 419
- pneumonitis, (1943) 273
- pulmonary embolism, (1939) 419
 - diagnosis, radiography in, (1939) 419
- treatment,
 - pneumonecctomy, (1943) 272
 - recent advances, (1943) 272
 - surgical, (1944) 295
- tuberculosis, (1939) 411 *See also Tuberculosis, pulmonary*
 - artificial pneumothorax with chlorine gas, (1939) 414
 - bilateral collapse therapy, (1939) 413
 - cerebral paratuberculosis, (1939) 412
 - clinical picture, (1939) 411
 - diagnosis, (1939) 412
 - haemoptysis, frequency and severity of, (1939) 411
 - newer methods of diagnosis, (1939) 113
 - lobectomy and pneumonecctomy, (1939) 414
 - pleural cavity, rupture into, (1939) 412
 - pneumococcal pneumonia complicating, (1939) 415
 - M & B 693 treatment, (1939) 415
 - pneumothorax, relapse after, (1939) 414
 - primary pulmonary tuberculosis in children, (1939) 411
 - thoracoclysis, (1939) 412
 - thoracoplasty, (1939) 413
 - treatment, (1939) 412
 - formic acid, with, (1939) 414
 - newer and older methods of, (1939) 114
 - sodium benzoate, with, (1939) 415
- tumours, (1939) 415 *See also supra*
 - malignant, of lungs and bronchi, (1939) 415
 - aetiology, (1939) 415
 - carcinoma, (1939) 115, 415
 - diagnosis, (1939) 416
 - prognosis, (1939) 416
 - thoracoscopy, (1939) 416
 - treatment, (1939) 416
 - radium in, (1939) 417
 - surgical, (1939) 416
 - X-ray, (1939) 416
- Lungs and pleurae diseases, (1939) 112
 - diagnosis, newer and older methods of, (1939) 112
 - treatment, newer and older methods of, (1939) 114
- Lupus erythematosus, (1941-2) 299
 - atypical verrucous endocarditis combined with, (1941-2) 250
 - clinical types, (1941-2) 299
 - disseminated type, (1940) 396, (1943) 348
 - clinical picture, (1940) 396
 - X-ray therapy, (1940) 396
 - hypertrophicus et profundus, (1943) 273
 - lymphatic glands, enlarged, in, (1944) 296
 - morbid anatomy, (1944) 296
 - renal involvement, (1941-2) 299
 - streptococci, (1940) 396
 - systemic, compared with dermato-myositis, (1941-1942) 309

Lupus erythematosus—continued

- treatment,
 - bismarsen, (1943) 273
 - gold treatment and chemotherapy, (1943) 273
 - rubiazol, with, (1940) 396
 - sulphonamides, with, (1940) 395, (1941-2) 118, 299
- Lupus vulgaris, (1939) 420, (1941-2) 299
 - starch injection in, (1939) 420
 - treatment by Grasset's tubercle endotoxoid, (1941-2) 300
- Lutocyclin, (1943) 95
- Lutogyl, (1943) 95
- Lygranum, (1941-2) 109
 - antigen for Frei test, (1943) 92
- Lymphadenopathy, giant follicular, (1940) 343; (1943) 275
- Lymphangiio-endothelioma, of uterus, (1943) 373
- Lymphatic glands,
 - diseases, (1940) 396, (1941-2) 300
 - tuberculosis adenitis, gelatin-acriflavine and calcium chloride treatment of, (1939) 420
 - tumours, classification of, (1939) 420
 - X-ray therapy in, (1940) 6
- enlargement,
 - lupus erythematosus, in, (1944) 296
 - non-infective, (1940) 396
- fat, in, (1941-2) 300
- giant follicular adenopathy, (1943) 275
- inflamed areas, in, (1941-2) 300
- lymphoid tumours, primary solitary, (1943) 274
- lymphosarcoma, (1943) 274
- cutis, (1943) 274
- new growths, (1940) 397

vessels,

- diseases, traumatic chylothorax, (1943) 276
- diseases and injuries, (1939) 431
 - elephantiasis, intra-arterial glycerin injection in, (1939) 421
- Kondoléon's operation for chronic lymphoedema, (1943) 275
- obstruction, (1940) 397
- Lymphoblastoma, (1944) 285
 - follicular, (1940) 397
 - spinal cord, of, (1944) 377
- Lymphocyte count, differential, in whooping-cough, (1943) 380
- Lymphocytoma, (1939) 540
- Lymphoedema
 - arm, of, (1940) 397
 - chronic, Kondoléon's operation for, (1943) 275
 - idiopathic, (1940) 427
- Lympho-epithelioma, thymus gland of, (1944) 383
- Lymphogranuloma
 - inguinale, (1941-2) 109 *See also Lymphopathia venereum*
 - diagnosis, (1941-2) 109
 - ocular, (1941-2) 109
 - sulphonamides in, (1939) 155
 - treatment, (1941-2) 109
 - venereum
 - lymphopathia venereum, (1943) 92
 - mode of transmission, (1943) 227
 - sulphonamides in, (1943) 227
- Lymphoid tumours, primary solitary, (1943) 274
- Lymphopathia venereum, (1939) 421, (1940) 92, 398; (1941-2) 300, (1943) 92
 - aetiology, (1939) 421
 - alimentary tract, infection of, (1941-2) 300
 - anthomaline in treatment, (1939) 422
 - bony changes, (1940) 398
 - cervical and inguinal glands, simultaneous enlargement of, (1940) 398
 - clinical picture, (1940) 398, (1941-2) 300
 - conjunctivitis, chronic unilateral, due to virus of, (1941-2) 300
 - diagnosis, (1939) 422
 - elephantiasis, (1940) 398
 - Frei reaction and bowel antigen, (1939) 422
 - history, (1944) 296
 - inguinal adenitis due to, (1941-2) 300
 - morbid anatomy, (1940) 398
 - pathology, (1944) 296
 - swallowing of virus in, (1941-2) 300

CUMULATIVE INDEX

Lymphopathia venereum—continued

- treatment, (1940) 398; (1944) 296
 - filtrates from infected glands, (1940) 399
 - M & B 693, with, (1939) 422
 - sulphanilamide, with, (1939) 17, 422; (1940) 398
 - sulphapyridine, (1940) 398
 - sulphonamides, with, (1941-2) 300
 - X-ray, (1940) 399
- ulcerative colitis, relation to, (1941-2) 193
- Lymphopenia, concussion, after, (1940) 251
- Lymphosarcoma, (1944) 285
 - bone lesions, (1944) 252
 - cutis, (1943) 274
 - prognosis, (1943) 274
 - prostate gland, of, (1943) 313
 - treatment, (1941-2) 300
 - X-ray, (1944) 253
- Lyophile plasma, infantile diarrhoea treated with, (1943) 188
- Lysholm grid, (1940) 103

M

- M 541 (sulphanilamide ethylsulphonate), (1940) 133
- M & B 693 *See also* Sulphapyridine
 - arthritis, in, (1939) 230
 - cerebrospinal fever, in, (1939) 274, 276
 - chemistry and pharmacology of, (1939) 170
 - Corynebacterium diphtheriae*, action on, (1941-2) 341
 - gonorrhoea, in, (1939) 356
 - meningitis, in, (1939) 125
 - pneumococcal, in, (1939) 427
 - plague, in, (1939) 479
 - pneumococcal pneumonia complicating pulmonary tuberculosis, (1939) 415
 - prophylaxis of cerebral abscess, (1939) 126
 - staphylococcal septicaemia, in, (1939) 530
- M & B 760 *See* Sulphathiazole
- Macrogenitosomia praecox, in one twin, (1940) 152
- Macrophages, interaction of fibroblasts and sarcoma cells with, (1940) 569
- Maffucci's syndrome, (1944) 162
- Maggot therapy
 - osteomyelitis, in, (1939) 254
 - wounds, in, (1940) 352
- Maggots, application of active principle of, (1939) 473
- Magnesium
 - glutamate, thyroid diseases treated with, (1940) 317
 - industrial hazards, (1944) 386
 - metabolism, (1940) 114
 - nephritis, in, (1940) 114
 - silicate granuloma, (1944) 208
 - sulphate, acute nephritis treated with, (1941-2) 312
 - convulsive shock therapy, use in, (1943) 317
 - pruritus vulvae treated with injections of, (1940) 593
 - renal failure, in, (1940) 114
 - uraemia, pre-operative treatment of, with, (1943) 372
 - tetany, in, (1940) 114
 - trisilicate, (1939) 168
 - duodenal ulcer, in treatment of, (1939) 47
 - hyperchlorhydria, in, (1939) 377
 - peptic ulcer treated with, (1939) 469, (1940) 441, (1941-2) 328
- Magnetotherapy, (1941-2) 217
- Malaria, (1939) 423, (1941-2) 96, 301, (1943) 82, 276
 - aetiology, (1941-2) 301
 - benign tertian, (1944) 297
 - blackwater fever complicating, (1943) 83
 - blood, subcutaneous injection of, conveyed by, (1940) 222
 - children, in, (1940) 399
 - clinical
 - picture, (1944) 297
 - types, (1943) 276
 - diagnosis, (1941-2) 301; (1943) 83, 276
 - respiratory affections, from, (1939) 423
 - differential diagnosis from acute abdominal disease, (1940) 400
 - epidemiology in war areas, (1941-2) 96

Malaria—continued

- immunity and premunition, (1939) 143
- incidence, (1944) 96
- malignant subtertian, (1944) 297
- parasites, rapid staining technique, (1941-2) 301
- parasitology, *Plasmodium ovale*, (1943) 276
 - positive syphilitic reactions in, (1943) 88
- prevention, (1944) 96
 - regional measures, (1944) 96
- prophylaxis, (1940) 75; (1941-2) 97
- recent work on, (1944) 96
- splenomegaly, chronic, following, (1940) 541
- survey of, (1939) 142
- transmission,
 - blood transfusions, by, (1941-2) 97
 - hypodermic syringes, by, (1941-2) 301
 - stored blood, in, (1941-2) 301
- treatment, (1939) 423, (1941-2) 98, (1944) 97
 - atebrin, (1939) 423
 - mepacrine, and, (1943) 82, 277
 - quinine compared with, (1939) 423
 - bistovol as adjuvant in, (1943) 292
 - chemotherapy, (1939) 144
 - chunine, (1943) 277
 - cinchona febrifuge, (1939) 424
 - control of, (1941-2) 98
 - drugs, survey of, (1944) 297
 - general paralysis of insane, in, (1941-2) 315, (1943) 292
 - 'cerebral impaludation', (1939) 447
 - mapharside, (1943) 83
 - mepacrine hydrochloride, (1940) 136
 - mycosis fungoides, in, (1943) 286
 - neurosyphilis, in, (1940) 400
 - pamaquin, in, (1940) 136, (1943) 82, 278
 - protosol, with, (1939) 424
 - prophylactic, (1943) 82, 278
 - quinine,
 - bihydrochloride, with, (1943) 277
 - intravenous, (1940) 400
 - sinine, (1943) 83, 277
 - sulphathiazole, effect of, on rigors, (1941-2) 301
 - sulphonamides in, (1940) 76
 - thio-bismol controlling, (1939) 424, (1941-2) 301
 - totaquina, (1943) 278
 - undesirable symptoms, control of, (1941-2) 301
 - war, and, (1940) 75, (1943) 82, 277
- Malignancy
 - breast cancer, new classification of, (1943) 163
 - diagnosis by biochemical methods, (1941-2) 183
 - gradation of, (1943) 370
 - sedimentation of red cells in, (1941-2) 163
- Malignant disease, (1940). *See also* Cancer, Intestinal obstruction Stomach; Tumours and some other conditions
 - soldiers, in, (1943) 12
 - treatment, surgical, (1943) 13
- Malingering, (1940) 400, (1944) 79
- effort syndrome, rare in, (1943) 231
- Forces, in, (1944) 297
- night-blindness, tests for, (1943) 207
- Malnutrition, forcing of fluids, (1940) 301
- Manchineel poisoning, (1939) 199
- Mandelic acid, (1941-2) 112
- B. coli* infections, in, (1939) 285
- excretion in breast milk, (1941-2) 262
- pyelitis, in, (1939) 159
- typhoid fever treated with, (1943) 202
- vulvo-vaginitis, in, (1940) 320
- Mandible
 - congenital hypoplasia of, (1940) 224
 - subperiosteal giant-cell tumour, (1940) 228
 - tuberculosis, (1940) 226
- Manganese, poisoning by, (1940) 560
- Mania
 - acute delirious, salt treatment of, (1939) 119
 - convulsive therapy, (1940) 57
- Manic excitement, shock treatment of, (1939) 118
- Mantoux test
 - tuberculin patch test, and, (1941-2) 292
 - tuberculosis, for, (1940) 568

CUMULATIVE INDEX

- Maparsen**
liver, effect on, (1940) 549
malaria treated with, (1940) 76
syphilis treated with, (1940) 548
- Maparside**
after recovery from arsphenamine dermatitis, (1941-2) 332
malaria, in, (1940) 76, (1943) 82
syphilis, in, (1940) 87, 90, (1941-2) 404
- Marble bones**, (1941-2) 171; (1943) 159
- March**
fracture, bilateral, (1941 2) 211
haemoglobinuria, (1943) 4
- Marchiafava-Micheli syndrome**, (1940) 172, (1941-1942) 140
- Mare's serum**, male sterility treated by pregnant, (1941-2) 400
- Marfan's syndrome**, (1943) 159
- Marhuana**, addiction to, (1939) 318
- Marmite** in tropical megalocytic anaemia, (1939) 204
- Marriage**
infertile, causes of, (1943) 352, (1944) 379
mental disease and, (1940) 57
- Masculinization**, adrenal cortical tumour of ovary, associated with, (1940) 156
- Masculinizing tumours of ovary**, (1943) 294
- Mass radiography**, (1940) 6, 503, (1941 2) 75, (1943) 2, 319, 324, (1944) 68
industrial medicine, in, (1944) 68
pulmonary tuberculosis, in, (1944) 68
recent work on, (1944) 68
tuberculosis, role in control of, (1944) 69
- Mastitis**
acute, lactation, of, (1940) 231
chronic, (1940) 231
interstitial, endocrine aetiology of, (1943) 165
X-ray therapy, (1940) 104
testosterone inunction in, (1941-2) 175
plasma-celled, (1943) 163
testosterone propionate therapy, (1940) 231
- Mastodynia**
hormone therapy, (1940) 132
testosterone propionate in, (1940) 132
- Mastoidectomy**, effect on hearing, (1940) 285
- Mastoiditis**, acute, mortality in children, (1943) 198
- Mastopatia**, hormone therapy, (1944) 52
- Maternal**
mortality,
age, influence of, (1944) 298
nutrition and, (1944) 142
primigravidae, elderly, complications in, (1944) 298
nutrition, (1939) 29; (1940) 16, (1944) 22
haemorrhage in the new-born, and, (1940) 16
- Measles**, (1939) 424, (1941-2) 302, (1944) 298-301
complications, (1941 2) 302, (1944) 298
virus infection, by, (1939) 424
convalescent serum, (1944) 300
jaundice after use of, (1944) 35
diagnosis, (1941 2) 68
encephalitis, (1944) 298, 301
paraplegia complicating, and, (1941 2) 302
encephalo-myelitis after, (1939) 328
epidemiology, (1944) 299
giant cells in prodromal stage, (1940) 401
haemorrhagic, (1944) 298
immune globulin, (1944) 300
immunization, (1939) 16, 425, (1944) 300
incidence, (1943) 49
mortality, (1944) 299
pathology and morbid anatomy, (1940) 401
placental extract,
convalescent serum in, and, (1941-2) 302
prophylaxis, in, (1939) 425
prevention by human cord serum globulin, (1943) 279
prophylaxis, (1941-2) 68, 302
specific, (1939) 77
purpura complicating, (1941 2) 302
treatment, (1941-2) 68, (1944) 299-301
results of, (1944) 299
sulphonamides, (1944) 299
virus, (1944) 299
- Meatal stenosis**, (1940) 574
- Mecholyl**. *See also* Acetyl- β -methylcholine bromide
action and composition of, (1939) 166
familial periodic paralysis, in, (1939) 166
glaucoma, in, (1939) 350
- Meckel's diverticulum**
carcinoma, primary, of, (1943) 102, 254
clinical picture, (1940) 279
perforation of ileum opposite, (1943) 102
ulceration of, (1940) 279
- Median mental sinus**, (1940) 412
- Mediastinal flutter**, (1941-2) 302
- Mediastinum**
diseases, (1939) 426, (1941 2) 302, (1943) 58, (1944) 301
tumour metastasis compressing brachial plexus, (1939) 425
- emphysema**,
spontaneous, (1944) 301
war injury causing, (1944) 302
- ganglioneuroma**, (1941-2) 303
- sympathogonioma of anterior superior**, (1944) 381
- traumatic lesions**, (1941-2) 302
- tuberculosis**, (1941-2) 302
- tumours**, (1941 2) 303
- Medical**
practitioner, State and national health, in relation to, (1939) 10
research, future of, (1940) 7
- Medicine**
advances in, (1941-2) 1
human factor in, (1940) 8
research in, (1940) 7
tropical, advances in, (1944) 96
- Medico-legal**
aspects in anaesthetics, (1939) 212
examinations and reports, (1939) 426
blood on nail parings, (1940) 401
estimation of age from teeth and jaws, (1941-2) 303
spermatozoa in seminal stains, detection of, (1939) 426
- Medinal and luminal**, prolonged narcosis induced by, (1939) 442
- Medulla oblongata**, tumours of, (1940) 230
- Megacolon**
acetyl- β -methylcholine bromide, in, (1940) 402, (1941-2) 303
acetylcholine as diagnostic test of utility of sympathectomy, (1940) 402
anal achalasia, and, (1939) 426
aetiology and treatment, (1939) 426
congenital,
anaesthesia in treatment of, (1940) 146
mechanism of, (1940) 146
- Megalocytic anaemia**. *See* Anaemia, megalocytic
- Meigs's syndrome**, (1944) 314
- Meinicke flocculation test**
tuberculosis, in, (1941 2) 414
Wassermann reaction, comparison with, (1940) 547
- Melaena**
amount of blood necessary to cause, (1940) 439
neonatorum, treatment, evaluation of, (1943) 230
- Melancholia**, involutional
endocrines in, (1941-2) 365, (1944) 347
hypopituitarism and, (1944) 347
oestradiol benzoate in, (1940) 488
treatment, (1941 2) 191
convulsion therapy, (1940) 58, (1941 2) 79
- Melano-carcinoma of adrenal gland**, (1941-2) 133
- Melanoma**
choioid, of, (1943) 374
conjunctiva, malignant, of, (1941 2) 196
ovary, of, (1943) 295
spinal cord, of, (1940) 536
subungual, (1940) 418
vagina, of, (1939) 601
xanthoma, cutaneous, and, (1940) 534
- Meliorheostosis**, (1944) 163, 231
- Membranes**, foetal
high puncture of, (1941-2) 279
induction of labour by rupture of, (1940) 374
test for rupture of, (1940) 372
- Memory**
defects after leptazol therapy, (1941 2) 367
disturbance of, after convulsion therapy, (1940) 491

CUMULATIVE INDEX

Menaphthone, (1941-2) 113, (1943) 94
 Ménière's syndrome, (1943) 38, 376, (1944) 404
 aetiology, (1943) 38
 deafness and, (1944) 404
 Eustachian tube obstruction causing, (1943) 376
 tinnitus, persistence of, after operation, (1944) 404
 treatment, (1939) 88; (1940) 584
 alcohol injection, (1943) 39, 376
 ammonium chloride and potassium nitrate, (1940) 584
 histamine, (1941-2) 422, (1943) 39, 377
 intravenous injection, by, (1940) 584
 potassium intake, high, (1940) 584
 sodium-free diet, (1943) 39, 377
 surgical, (1940) 584, (1943) 39
 vitamins, with, (1940) 584
 Meningeal symptoms,
 epidemic myositis causing, (1943) 5
 T A B vaccine causing, (1943) 282
 washing in cerebrospinal fever, (1939) 276
 Meningitis, (1939) 426
 acute aseptic leptomeningitis, (1943) 279
 anthrax causing, (1940) 188
 benign lymphocytic, (1940) 406
 cerebrospinal fever, in, (1943) 172
 cerebrospinal fluid, chloride in, (1940) 406
 diagnosis from tularemia, (1941-2) 415
 influenzal, sulphapyridine in, (1940) 404, (1941-2) 305
 meningococcal, (1939) 429 *See also* Cerebrospinal fever
 serum and sulphanilamide treatment, (1939) 17, 275, 429
 mumps complicated by, (1939) 436
 non-bacterial, (1939) 429
 otogenous, (1941-2) 217
 Pfeiffer's bacillus causing, (1943) 279
 pneumococcal, (1939) 426
 bacteriology of infantile, (1939) 426
 chemotherapy in, (1943) 280
 recurrent, (1940) 404
 sulphapyridine in, (1940) 402-4
 serum therapy and, (1940) 404
 surgery and vaccines, (1939) 427
 treatment, (1940) 402-4
 sulphonamides, (1939) 125, 171, 427
 antiserum, and, (1941-2) 304
 pyogenic, (1939) 428
 aetiology, (1939) 428
 treatment,
 sulphapyridine, (1941-2) 304
 sulphonamide, (1939) 88, 428
 surgical, (1939) 428
 septicaemia, purpura and adrenal haemorrhage associated with, (1941-2) 186
Streptococcus viridans causing, treated by sulphapyridine, (1941-2) 304, 305
 treatment, (1943) 279
 chemotherapy, (1941-2) 58
 tuberculous,
 diagnosis, (1940) 405
 Levinson's test, (1940) 405
 Meningocele, cranioleucania associated with, (1941-2) 396
 Meningococcal endocarditis, without meningitis, (1941-2) 250
 Meningococcal septicaemia, (1941-2) 4
 Meningococcus
 adrenal haemorrhage caused by, (1941-2) 132
 infection without meningitis, (1943) 172
 M & B 693, effect of, (1940) 134
 septicaemia caused by, (1943) 172
 sulphanilamide in, action of, (1940) 133
 sulphonamides in, action of, (1939) 170
 Meningo-encephalitis, mumps complicated by, (1943) 282
 Meningo-encephalo-mylitis, post-vaccinal, (1943) 201
 Menisci, removal of, in internal derangement of knee, (1940) 361
 Meno-metrorrhagia, oestriol and pregnenolone therapy, (1940) 407
 Menopausal arthritis, (1940) 199-201
 oestrogenic therapy, (1940) 201
 E.M.S. II

Menopause *See* Climacteric
 Menorrhagia, (1939) 430
 treatment, (1944) 302
 autohaemotherapy, (1939) 430
 oestriol and pregnenolone, (1940) 407
 oestrogen and progesterone, (1939) 430
 X-ray, (1939) 430
 Menorrhagia and metrorrhagia, (1939) 431
 testosterone propionate in, (1939) 431
 Menstruation, (1943) 19
 anovular, (1944) 26
 blood electrolytes and, (1941-2) 163
 constitutional types and, (1940) 339
 delayed, prostigmin in, (1940) 166
 disorders,
 hormone therapy, (1940) 132, (1943) 96, 334, (1944) 51, 369 *See also* Hormone therapy, Hormones
 sex hormone therapy, (1941-2) 384
 stilboestrol in, (1940) 132
 intermenstrual pain, (1941-2) 21
 oedema of lung associated with, (1941-2) 318
 oestrogens and, (1941-2) 21
 pregnanediol excretion, (1940) 21
 safe and fertile periods, (1944) 379
 salivary syndrome, premenstrual, (1940) 434
 testosterone propionate and, (1940) 132, 526, (1941-2) 21
 Mental deficiency, (1939) 431, (1940) 407
 arhinencephaly, (1940) 408
 associated skin diseases, (1939) 431
 creatine-creatinine excretion, (1940) 407
 mongolism, (1939) 432, (1940) 408
 aetiology, (1939) 432
 thyroid and pituitary in, (1939) 432
 Mental disease, (1939) 15, 116, (1941-2) 79 *See also* Psychoses
 aetiology, (1943) 65, 314
 age incidence, (1940) 56
 amines, toxic, (1940) 54
 carbon disulphide intoxication causing symptoms of, (1943) 365
 cerebral circulation in, (1940) 56
 endocrinological researches, (1940) 55
 hyperthyroidism in, (1943) 316
 incidence, (1940) 56
 increase in, (1940) 57
 industry, in, (1943) 69
 liver function tests in, (1940) 55
 male sex hormones in, (1940) 525
 management in practice, (1944) 76
 marriage and, (1940) 57
 morbid anatomy, (1939) 116
 narcoses, prolonged, in, (1939) 442, (1940) 418
 parathyroidectomy causing, (1940) 54
 prognosis, (1944) 75
 recent work on, (1940) 54, (1944) 72
 sodium amytal in, (1940) 59
 statistics, (1940) 56
 toxins causing, (1940) 54
 treatment,
 acute manic excitement, of, (1939) 119
 leucotomy, (1944) 72
 frontal, (1943) 67, 316
 shock therapy, (1939) 116, (1940) 57, 59, 494, (1941-2) 218, (1943) 66, 317, (1944) 73
 convulsion, (1940) 57, 59, 494
 electrical, (1941-2) 218, (1944) 73
 insulin, (1944) 73
 surgical treatment, (1944) 72
 vitamins and, (1940) 56
 deficiency in, (1943) 64
 war, influence of, (1941-2) 363, (1943) 68; (1944) 78 *See also* Effort syndrome
 Mental disorders
 biochemical mechanisms, (1941-2) 84
 leucotomy, frontal, (1941-2) 81
 nitrogen balance in, (1941-2) 84
 organic, (1941-2) 84
 sex hormones, role of, (1941-2) 364
 treatment,
 convulsion, (1941-2) 79
 electrical, (1941-2) 80
 hormone, (1941-2) 81

CUMULATIVE INDEX

Mental disorders—continued treatment—continued

- insulin shock, (1941-2) 81
- surgical, (1941-2) 81
- Mental**
 - hygiene, (1944) 75
 - sinus, median, (1940) 412
 - symptoms,
 - blast causing, (1944) 79
 - narcolepsy, in, (1941-2) 311
 - neurosyphilis, in, (1941-2) 316
- Menthol**, allergy to, (1939) 199
- Mepacrine**
 - hydrochloride, (1940) 76, 127
 - malaria, in, (1940) 136, (1943) 82, 277
 - methanesulphonate, (1940) 127
- Meprochol**, (1944) 110
- Mercupurin**, death following intravenous injection of, (1944) 385
- Mercurial**
 - diuretics, (1943) 1
 - fatalities, investigation of, (1944) 323
 - heart failure, in, (1939) 20, 60, (1941-2) 253
 - nephrosis, in, (1943) 290
 - oedema, in, (1940) 5
 - poisoning by, (1944) 385
 - rash, (1939) 319
- Mercuric**
 - oxycyanide in gonorrhoea, (1940) 318
 - poisoning, (1940) 555
 - sulphide in pruritus ani, (1940) 189
- Mercurochrome**
 - pyelonephritis, in, (1939) 384
 - sterilization of oral mucous membrane, in, (1939) 384
- Mercury**
 - colloidal silver and, in venereal prophylaxis, (1940) 450
 - compounds in sterilization of instruments, (1939) 384
 - cystoscopy, after, (1940) 555
 - fulminate, poisoning by, (1940) 559
 - generalized exfoliative dermatitis caused by, (1943) 364
 - intravenous injection in nephrosis, dangers of, (1943) 290
 - ointment, ammoniated, idiosyncrasy in children, (1941-2) 332
 - organic compounds, poisoning by, (1941-2) 411
 - poisoning, (1940) 550, 559, (1943) 364, (1944) 385
 - sodium formaldehyde sulphonylate therapy, (1940) 555
 - sulphide, tattoo for leucoplakia vulvae, (1941-2) 430
 - syphilis, in, (1941-2) 404
- Mersalyl**, (1943) 1
- Mescaline**
 - psychoses produced by, (1940) 54, 496
 - schizophrenic symptoms produced by, (1940) 496
- Mesenteric**
 - thrombosis and embolism, (1941-2) 125
 - vascular occlusion, (1941-2) 125
- Mesentery**, sensitiveness of, (1940) 141
- Mesodermal**
 - angioma of eye, (1943) 205
 - tumours, mixed, of uterus and vagina, (1940) 577
- Mesonephroma of ovary**, (1943) 295
- Mesulphen**, (1943) 94
- Metabolic conditions**, skin disease associated with, (1939) 65
- Metabolism**, (1941-2) 305
 - basal, (1939) 432
 - blood cholesterol, relation to fall in, (1939) 432
 - hypothyroidism and hyperthyroidism, in, (1941-2) 306
 - benzedrine, effect of, (1940) 449
 - brain, (1943) 64
 - carbohydrate,
 - adrenal cortex and, (1943) 280
 - fat, and, (1943) 32
 - infection, and, (1941-2) 306
 - Crohn's disease, in, (1941-2) 200
 - disordered,
 - dermato-mycosis, in, (1941-2) 309
 - psoriasis, in, (1941-2) 362

Metabolism—continued

- fat, (1944) 303
- skin diseases, in, (1944) 375
- haemoglobin, (1943) 25
- inorganic salts, (1943) 213
- mineral, (1940) 113
- pituitary growth hormone, effects of, (1943) 302
- serum proteins, (1941-2) 305
- Metacresyl acetate** and thymol, otomycosis treated with, (1940) 284
- Metaphen** in sterilization of oral mucous membrane, (1939) 384
- Metastases**
 - carcinomatous, confined to scalp, (1940) 535
 - kidney, in, (1941-2) 277
 - ureteral, (1941-2) 278
- Metatarsal bone**, supernumerary, (1941-2) 232
- Methaemalbumin**, (1941-2) 7, 170; (1943) 83
- Methaemoglobin**, (1941-2) 7
- Methyl**
 - alcohol poisoning, (1943) 110
 - chloride, poisoning by, (1941-2) 411
 - mercury compounds, poisoning by, (1941-2) 411
 - salicylate, corneal ulcers treated with, (1939) 292
 - testosterone, (1943) 96
 - eunuchism treated with, (1941-2) 385
 - gynaecology, in, (1944) 27
 - hepatic inactivation of, (1944) 369
 - impotence treated with, (1943) 335
 - inhibition of lactation by, (1943) 335
 - puerperal engorgement of breasts treated with, (1944) 352
- Methylcholanthrene**, carcinogenic action of, (1940) 239
- Methylene blue**
 - cyanosis treated with, (1939) 295, (1940) 120, 133
 - reaction of red cells, (1939) 245
 - sodium ricinoleate and, in otosclerosis, (1940) 255
- Metrazol**, (1939) 164 *See also* Cardiazol, I eptazol
- Metrorrhagia**
 - oestrol and pregnenmonol in, (1940) 407
 - testosterone propionate in, (1940) 20
 - treatment,
 - radium, (1944) 303
- Meulengracht**
 - regime, peptic ulcer treated by, (1941-2) 328
 - treatment for haematemesis, (1943) 300
- Mice**, cancer in, (1940) 7
- Micrococcus albicans**, black hairy tongue caused by, (1941-2) 308
- Micro-organisms**, effect of milk on, (1939) 381
- Micro-telephones for the deaf**, (1939) 100
- Midbrain**, tumours of, (1940) 230
- Middle ear**
 - cholesteatomas, (1943) 199
 - disease, intracranial complications of, (1939) 87
 - petrositis, aetiology and surgery, (1943) 199
 - Schuller-Christian syndrome involving, (1941-2) 287
 - suppuration,
 - chronic, argyrol displacement in, (1940) 284
 - extra-dural abscess caused by, (1941-2) 216
 - facial paralysis complicating, (1944) 219
- Migraine**, (1939) 433, (1941-2) 90, 306
- actiology**, (1940) 408, (1941-2) 306
- biochemical aspects of**, (1943) 281
- clinical picture**, (1940) 408
- diagnosis**, (1941-2) 307
- ergotamine tartrate therapy**, (1939) 20
- complications of**, (1939) 434
- headache caused by**, (1941-2) 91; (1944) 247
- hemiparesis associated with**, (1940) 408
- hypertension, relation to**, (1941-2) 306
- hypertonic saline solution treatment**, (1939) 433
- hypothyroidism**, associated with, (1939) 433
- neuralgia, migrainous**, (1941-2) 307
- neurosis, recurrent pyrexia and**, (1944) 346
- oxygen inhalation**, (1939) 433
- pilocarpine for eye symptoms**, (1939) 433
- sympathetico-adrenal mechanism in**, (1943) 280

CUMULATIVE INDEX

- Migraine**—*continued*
treatment, (1940) 409
ergotamine tartrate, (1940) 409
menopause, induced, (1940) 409
oxygen,
concentrated, (1940) 409
inhalation, by, (1941-2) 307
sex hormones, with, (1940) 409
vitamin B₁, with, (1940) 409
tumour in calcareine fissure causing, (1940) 408
Migrainous neuralgia, alcohol treatment, (1941-2) 307
Mikulicz's cells in rhinoscleroma, (1943) 328
Milk
abortion fever caused by, (1940) 143
gastro-intestinal allergy due to, (1941-2) 138
human,
antirachitic value of, (1940) 346
excretion of mandelic acid in, (1941-2) 262
excretion of sulphamylamide in, (1940) 458
properties of, (1939) 381
raw, abortion fever caused by, (1940) 143
scarlet fever transmitted by, (1943) 328
secretion,
control of, (1939) 35
disturbances of, (1939) 222
lactogenic hormone action on, (1939) 109
spore-forming bacteria in, (1941-2) 232
Miller-Abbott tube, (1943) 252
diagnosis by, (1943) 102
intestinal obstruction treated by, (1940) 12, (1941-2) 272, (1944) 275
Milroy-Nonne disease, (1940) 427
Mine workers, hypopyon in, (1939) 290
Mineral
metabolism, (1940) 113
oil, laxatives and vitamin A deficiency, (1941-2) 426
Miner's nystagmus, prophylaxis by illumination, (1944) 313
Miners
bituminous coal, of, silicosis in, (1941-2) 389
vitamin A requirements of, (1941-2) 426
Miniature films, radiography, in, (1940) 103
Minor ailments, survey of, (1939) 16
Mint, dermatitis caused by, (1940) 259
Mite-typhus, (1940) 571
Mitigal, (1943) 94
Mitosis
histological observations on, (1944) 252
irradiation on, effect of, (1941-2) 416
uterine leiomyomas, in, (1944) 398
Mitral
stenosis,
ball thrombi, (1941-2) 252
rheumatic, (1941-2) 252
signs of early, (1941-2) 44
valve, stenosis, (1940) 336
clinical picture, (1944) 249
relative, (1944) 249
Mittelschmerz
ovulation and, (1944) 26
Mixed tumours, parotid gland, of, (1941-2) 323
Moccasin snake venom, herpes simplex treated by, (1941-2) 256
Mole, hydatidiform, (1941-2) 190
Molluscum contagiosum, (1940) 298
Mongolism, thyroid and pituitary in, (1940) 408
Monilia albicans, (1941-2) 285
endocarditis, subacute, caused by, (1943) 237, (1944) 250
Monilia
infections, (1943) 218
vaginitis, (1941-2) 284
Monoethanolamine
B. coli infection, in, (1939) 286
oleate, sensitivity to, (1941-2) 421
Monolate, sensitivity to, (1941-2) 421
Mononucleosis, infective *See* Glandular fever
Monorchia, (1941-2) 231
Morale, (1943) 69
air-raids, effects of, (1944) 341
individual, importance of, (1944) 342
Moranyl in trypanosomiasis, (1939) 146
Morgagni's syndrome, (1940) 467
Morphine
abstinence syndrome, (1943) 196
addiction, treatment by refrigeration, (1941-2) 350
cholinergic action on stomach, (1944) 323
injuries, use after, (1944) 271
relief of pain by prostigmin methylsulphate and, (1941-2) 338
Mortality rates, improvement in, (1939) 6, 9
infant, (1939) 37
Morvan's disease, (1939) 441
Mosquitoes
bites, hypersensitiveness to, (1940) 160
disease, carriers of, (1944) 156
Mosso's ergograph, in investigation of fatigue, (1943) 232
Mossy foot, clinical picture and diagnosis, (1944) 390
Motor cyclists, value of crash helmets for, (1943) 8, 250
Motor neurone diseases, (1940) 409, (1941-2) 307, (1943) 281, (1944) 304
Mountain sickness, arsenic as prophylactic, (1939) 280
Mouth
carcinoma, tobacco chewing and, (1941-2) 308
condition of, in hypoparathyroidism, (1941-2) 322
diseases, (1939) 434, (1940) 410-2, (1941-2) 307, (1944) 304
cancer of lip, (1943) 281
carcinoma, classification and treatment, (1939) 435
glossitis, epidemic, nicotinic acid therapy, (1939) 435
glossodynia, (1939) 434
infections of, chemotherapy in, (1941-2) 60
neurofibromatosis involving, (1943) 292
recurrent ulcers in genitalia and, (1943) 20
'sore' and vitamin B₂, (1941-2) 308
thrush in new-born infants, (1943) 218
Vincent's infection of, (1943) 2
Mucinous carcinoma of breast, (1941-2) 176
Mucous membrane
gastric, presence of spirochaetes in, (1941-2) 401
nasal, anti-polio-myelitic substances from, (1941-2) 356
Mule-spinner's cancer, (1941-2) 392
Multinucleosis among Bantus, (1941-2) 416
Mumps, (1939) 435
complications, (1939) 436, (1944) 305
meningitis, (1939) 436
meningo-encephalitis, (1943) 282
neurological, (1940) 412
nervous system in, (1941-2) 309, (1943) 282
oedema of epiglottis in, (1944) 305
pathology, (1939) 435
polyradiculitis, myelitis and herpes zoster complicating, (1941-2) 309
pre-sternal swelling in, (1944) 305
Mural thrombi, as source of emboli, (1941-2) 218
Murmur
Austin Flint's presystolic, (1943) 239
cardiac, (1940) 5
functional, (1941-2) 45
systolic, causes, (1944) 247
Muscle
desmoid tumour of, (1943) 184
diseases, (1939) 436, (1940) 412-7, (1941-2) 309, (1943) 282, (1944) 305
carbohydrate metabolism, (1939) 437
creatine metabolism, (1939) 439
dystonia musculorum deformans, (1939) 438
quinine in treatment, (1939) 438
epidemic myositis, (1943) 282
myotonia congenita (Thomsen's disease), (1939) 437
differential diagnosis, (1939) 437
quinine in treatment, (1939) 437
myotonia strophica, (1939) 438
heredity, (1939) 438
vibration sense, disturbance of, (1939) 438
persistent myalgia, (1943) 283
potassium in relation to, (1940) 68
progressive muscular dystrophy, (1939) 436
creatine metabolism, (1939) 436
glycocoli, treatment with, (1939) 437

CUMULATIVE INDEX

Muscle—continued

diseases—continued

pseudo-hypertrophic muscular dystrophy, (1939) 436

pancreas in relation to, (1939) 436

treatment by vitamins E and B₆, (1941-2) 230, 426, (1943) 308

dystrophy. *See* Muscular dystrophy

extracts, effect on heart in shock, (1944) 370

fibrillation, peripheral origin of, (1941-2) 229

haemorrhage into, spontaneous, (1943) 282

hypertonia, haematoporphyrin in, (1940) 415

injuries, (1940) 413, (1944) 305

lipoma, (1941-2) 310

paralysis, electrotherapy of, (1943) 77

paresis, 'lowering the arm' sign in, (1940) 412

response to histamine, effect of vitamin C on, (1941-2) 425

tension, (1941-2) 84

tumours, (1941-2) 310

Muscular

atrophy, progressive, (1944) 304

dystrophy, (1941-2) 310

creatinine-coefficient and creatine-tolerance test, (1940) 414

pseudo-hypertrophic, vitamin B₆ in, (1940) 415

vitamin B₆ therapy, (1941-2) 428

vitamin E therapy, (1940) 70, 131, 414, (1941-1942) 5, 50, 426, 428, (1944) 89

wheat-germ oil in, (1940) 414

fatigue, amino-acetic acid and gelatin, effect of, (1941-2) 331

Muscularis mucosal, paralysis of, and sprue syndrome, (1941-2) 27

Mustard-gas

burns, (1943) 167

eye lesions,

clinical types of, (1943) 80, 220

treatment, (1943) 80, 221

eyes, effects on, (1940) 311

keratitis caused by, (1944) 192

Myalgia

acute, of neck and shoulders, (1944) 305

epidemic, (1943) 282

German measles, in, (1940) 312

idiopathic, (1941-2) 229

persistent after sore throat, (1943) 283

Myalgic spots, (1941-2) 229

scratches, in, (1944) 364

Myasthenia

guanidine, in, (1943) 285

thymectomy, in, (1943) 285

Myasthenia gravis, (1939) 439

clinical picture, (1939) 439

heart in, (1944) 306

hyperthyroidism, relation to, (1940) 416, (1943) 284

incidence in children, (1943) 283

myocardial changes in, (1944) 306

ocular manifestations, (1943) 284

periodic paralysis, relation to, (1940) 69

potassium in relation to, (1940) 68, 416

prostigmin in, (1939) 166, 439

ephedrine, and, (1939) 166

ptosis, monocular, in, (1943) 284

thymic enlargement, (1943) 284

thymic tumours in, (1943) 283, 362

thymus lesions in, (1940) 416

thyrotoxicosis associated with, (1943) 283

toxic goitre associated with, (1943) 224

treatment,

drugs, evaluation of various, (1940) 416

ephedrine and adrenaline, (1943) 285

eserine and prostigmin, (1943) 284

guanidine hydrochloride, (1940) 417

prostigmin, (1940) 417

Mycetoma, eyelid, of, (1940) 298

Mycobacterium leprae, (1941-2) 284

Mycobacterium tuberculosis, (1941-2) 284

blood charcoal, effect in cultivation, (1944) 393

cultivation and guinea-pig inoculation, (1944) 393

influence of silica on, (1940) 530

serial inoculation, (1944) 393

staining with auramine, (1943) 368

sulphonamide drugs, effect of, (1940) 457

Mycosis. *See also* Fungous diseases

Mycosis fungoides

aetiology, (1940) 417

Hodgkin's disease as sequel, (1943) 286

streptococcal infection in, (1940) 417

treatment by induced malaria, (1943) 286

Mydriatics, atropine, scopolamine, and homatropine-paredrine as, (1940) 449

Mydricaine, (1943) 147

Myelitis, mumps complicated by, (1941-2) 309

Myelography, iodized oil, with, (1941-2) 371

Myeloid

metaplasia, agnogenic, of spleen, (1940) 541, (1943) 351

sarcoma, (1941-2) 172

Myeloma

bone, of,

endothelial, (1943) 161

multiple, (1941-2) 173

solitary, (1941-2) 173

multiple, (1940) 227, (1944) 163

Myelomatosis, treatment, wide-field X-ray therapy, (1940) 105

Myelocleiosis, leukaemia, differentiation from, (1940) 32

Myeloscope, (1940) 67

Myiasis, (1939) 440, (1941-2) 310

larva migrans, mite found in, (1939) 440

Myocardial infarction, (1940) 185

acute, (1943) 125

rupture of interventricular septum due to, (1941-1942) 146

Myocarditis, (1941-2) 249

acute

interstitial, arsphepnamine causing, (1941-2) 332

isolated (Fielder's), (1943) 235

gonococcal, (1940) 333

subacute, of unknown aetiology, (1940) 333

vitamin B₁ deficiency and, (1940) 586

Myocardium

chemical changes in cardiac failure, (1943) 240

coronary thrombosis, in, (1940) 185

diseases, (1940) 333, (1941-2) 249

infection, pain in shoulder as sequel, (1941-2) 249

lesions, myasthenia gravis, in, (1944) 306

tumours, (1943) 235

Myoclonus

epilepsy, primary optic atrophy associated with, (1940) 295

palatal, (1940) 411

Myocytes in rheumatic inflammation, (1943) 327

Myohaemoglobinuria, acute paralytic, (1944) 245

Myoma, of epididymis, (1943) 203

Myomectomy, fibroids, for, (1944) 27

Myopia

sulphonamide therapy causing, (1941-2) 310

survey of, (1939) 129

treatment, calcium and vitamin D, (1940) 417, (1944) 306

Myositis, (1941-2) 309

dermato-myositis, (1940) 413

epidemic, (1944) 305

neuritis, erythema and meningeal symptoms, with, (1943) 5, 282

ossificans traumatica, (1940) 413

Myotonia

atrophica,

potassium in relation to, (1940) 68

prostigmin in, (1940) 68

congenita, diagnosis in infancy, (1940) 415

testosterone propionate in, (1940) 415

vitamin E therapy in, (1941-2) 426

Myxoedema, (1939) 440

aetiology, pituitary fibrosis in, (1939) 440

anaemia associated with, types of, (1939) 53

angina pectoris and, (1940) 182

anginal pain in, (1944) 307

atypical syndromes, (1939) 440

cardiovascular diseases associated with, (1943) 286

gonads in, (1939) 440

heart in, (1944) 307

hypertrophy of muscles, (1939) 441

hypopituitary, (1943) 286

metabolic changes in, (1943) 286

pretibial, in thyrotoxicosis, (1944) 307

Myxoma of larynx, (1943) 41

CUMULATIVE INDEX

- N**
- Naevi**
 radon gas in, (1939) 514
 thorium-X in treatment of, (1939) 539
- Naevus sebaceus and sebaceous carcinoma, (1943) 345**
- Nail lacquer and polish, dermatitis due to, (1941-2) 203, (1943) 183**
- Nails**
 absence of, with bony changes, (1941-2) 230
 blood on, medico-legal examination, (1940) 401
 diseases of, (1939) 441, (1940) 418, (1941-2) 311, (1944) 307
 carcinoma, (1939) 441
 paronychia, Morvan's disease, (1939) 441
 thumb nails, absence of, (1939) 441
 dystrophies, (1941-2) 311
 glomus tumour, (1941-2) 311
 health signal, as, (1944) 307
 lichen planus of nail-bed, (1941-2) 287
 longitudinal striation, (1941-2) 311
 new growth, (1941-2) 311
 onycholysis, (1940) 418
 psoriasis, X-ray therapy for, (1941-2) 362
 subungual melanoma, (1940) 418
 transverse lines, (1941-2) 311
 tumours, (1940) 418
 white spots on, (1944) 308
- Naphthalene**
 chlorinated, poisoning by, (1944) 387
 compounds, corneal penetration, rate of, (1944) 323
 exfoliative dermatitis due to, (1941-2) 204
 poisoning, (1940) 555
- Naphthoquinone, (1940) 31, 117**
 derivatives, vitamin K activity of, (1940) 31, 117, 590
- neonatal haemorrhage, in, (1940) 16**
- Narcolepsy, (1943) 287**
 mental symptoms, (1941-2) 311
- Narcotism, (1943) 121**
- Narcosis**
 basal, (1940) 177, (1941-2) 142, (1943) 121
 contra-indications and uses, (1944) 136
 pentothal sodium, (1944) 137
 brain metabolism and, (1940) 119
 foetal asphyxia and, (1940) 19
 prolonged, (1939) 442
 medinal and luminal, induced by, (1939) 442
 paraldehyde and dial, (1940) 418
 thrombophlebitis complicating, (1939) 442
- Nares, flattening of, in seventh nerve affections, (1939) 294**
- Nasal**
 choanae, congenital occlusion of, (1940) 144
 infections, antiseptic snuff for, (1943) 305
 medication, argyria following, (1940) 235
 mucosa,
 action of drugs on, (1940) 445
 antiseptic snuffs, action of, (1941-2) 331
 sepsis, acriflavine and proflavine in prevention of, (1941-2) 330
 septum, dermoid cyst of, congenital, (1941-2) 204
 sinuses *See* Sinuses, nasal accessory
- Nasopharynx**
 diseases, (1941-2) 317
 juvenile basal fibroma of, (1941-2) 317
 tuberculosis, differential diagnosis, (1940) 390
 tumours, (1941-2) 317
- National war formulary, (1941-2) 112**
- Nausea, stilboestrol therapy causing, (1944) 26**
- Navy**
 impetigo in, (1944) 257
 peptic ulcer in, (1944) 319
- Neck**
 cysts, (1941-2) 311
 myalgia, acute, of, (1944) 305
 tumours and other morbid conditions, (1939) 442, (1941-2) 311, (1943) 287
 carcinoma, metastatic, (1939) 442
- Necrobiosis lipoidica**
 diabeticorum, (1941-2) 395
 granuloma annulare, resemblance to, (1943) 347
- Necroscleritis nodosa, (1940) 254**
- Necrosis**
 fat, (1943) 250
 post-irradiation, (1941-2) 130, (1943) 43, 323
- Negroes, melanotic carcinoma in, (1940) 534**
- Nematode infections**
 intestinal, (1944) 308
 phenothiazine treatment, (1943) 287
- Nematode infestations, (1940) 419**
- Nematodes, (1941-2) 311**
 gastric cancer in animals caused by, (1940) 240
- Nembutal, (1939) 163**
- Neosarsphenamine**
 bronchiectasis, in, (1939) 266
 relapsing fevers, in, (1939) 147
 encephalitis, arsenical, caused by, (1944) 25
 intravenous drip method, (1940) 90
 neurosyphilis, in, (1941-2) 316
 staphylococcal infection, in, (1941-2) 342
 syphilis, in, (1940) 87, 90
 tick-bite fever, in, (1940) 86
 urethritis, in, (1941-2) 417
- Neocryl**
 neurosyphilis treated with, (1941-2) 317
 toxicity of, (1941-2) 317
- Neokharisvan, anthrax, in, (1941-2) 147**
- Neo-oestranol, (1940) 131**
- Neoprontosil**
 colitis, ulcerative, in, (1939) 296, (1940) 249
 keratitis, trachomatous, treated with instillations of, (1940) 565
 undulant fever, in, (1940) 573
 reduction in tissue suspensions, (1941-2) 343
- Neostebene, kala-azar, in, (1943) 256**
- Neostibosan, kala-azar, in, (1939) 148**
- Neosynephine**
 asthma, in, (1940) 203
 maintaining blood pressure during spinal anaesthesia, for, (1941-2) 142
 premedication, (1939) 209
 shock and collapse, in, (1940) 528
- Nephrectomy**
 life after, (1944) 279
 pressor response to renin, effect on, (1941-2) 166
 prognosis, (1944) 279
 unilateral, (1940) 370
- Nephritic convulsions, treatment with magnesium sulphate, (1943) 289**
- Nephritis, (1941-2) 312 (1943) 71, 288, (1944) 309**
See also Nephritis and nephrosis
- acute,
 glomerulo-nephritis, (1940) 5
 aetiology and treatment of, unsolved problems in, (1940) 5
 chemical pathology, (1940) 421
 children, in, (1940) 420
 acute, (1940) 420
 tonsillectomy, effect of, (1940) 422
 chronic,
 intestines, changes in, (1940) 420
 morbid anatomy, (1940) 420
 vicious circle in, (1941-2) 312
 classification, (1940) 420
 clinical manifestations and pathology, (1943) 71
 clinical picture, (1940) 421, (1941-2) 313
 course and prognosis, (1941-2) 313, (1943) 288
 glomerulo *See* Glomerulo-nephritis
 glomerulosclerosis, intercapillary, (1940) 421
 hypertension and, (1941-2) 312, (1943) 71, (1944) 310
 magnesium metabolism, (1940) 114
 morbid anatomy, (1941-2) 312
 pregnancy, in, (1940) 17
 scarlet fever, in, (1941-2) 313
 syphilis, relation to, (1940) 421
 tonsillectomy, and, (1944) 309
 prophylaxis and cure, in, (1940) 422
 treatment, (1940) 422, (1941-2) 313
 chemotherapy, (1943) 72
 magnesium sulphate, (1943) 289
 serum transfusions, (1943) 290
 surgical, (1943) 72
- Nephritis and nephrosis, (1939) 443**
 acute glomerulo-nephritis, (1939) 444
 acute nephritis, (1939) 443
 course and prognosis, (1939) 444

CUMULATIVE INDEX

Nephritis and nephrosis—*continued*
 haemorrhagic glomerulo-nephritis, amidopyrine
 in treatment of, (1939) 444
 pathology, (1939) 443
 pneumococcal peritonitis complicating, treat-
 ment of, (1939) 444

Nephrosclerosis
 desoxycorticosterone acetate producing, (1944)
 122
 pregnancy toxæmias and, (1941-2) 357

Nephrosis, (1939) 443, (1941-2) 312, (1943) 71,
 288. *See also* Nephritis and nephrosis
 basal metabolism, (1939) 443
 children, in, (1940) 421
 complement activity of blood, (1939) 443
 hypo-amino-acidaemia in, (1940) 421
 mercurial injections, intravenous, dangers of,
 (1943) 289
 treatment, (1940) 422, (1941-2) 313
 acacia, (1940) 422, (1941-2) 314, (1943) 288
 blood serum, concentrated human, (1940)
 422
 chemotherapy, (1943) 72
 vitamin A, (1941-2) 313

Nephrostomy, preliminary, in treatment of hydro-
 nephrosis, (1944) 277

Nephrotic syndrome, (1943) 288, 290
 hypertension in diabetes mellitus, with, (1941-2)
 205
 serum transfusion in, (1943) 31, 290

Nephro-ureterectomy, for primary carcinoma of
 ureter, (1941) 277

Neptal, (1943) 1
 heart failure, in, (1939) 60

Nerve
 cell, enzymes of, (1943) 74
 eighth, affections of, (1941-2) 199
 endings, adjustments of, (1944) 311
 grafts (1941-2) 95
 facial paralysis, in treatment of, (1939) 89
 impulses, transmission of, (1939) 122
 injury, (1943) 290, (1944) 17, 311
 microscopical changes, (1944) 311
 motor disturbances, (1944) 312
 recovery of motor functions after, (1944) 312
 repair of divided nerves by fibrin suture, (1944)
 311
 scleroderma and, (1940) 516

lesions,
 balneotherapy, (1943) 244
 leprosy, in, (1943) 264
 rheumatoid arthritis, in, (1944) 152

neuroma formation, prevention of, (1944) 91

paralyses, after local sulphonamide application,
 (1944) 312

peripheral,
 anatomy of, (1941-2) 88, (1943) 74
 grafting, (1941-2) 95
 motor recovery, (1944) 90
 pellagra, in, (1941-2) 324
 plasma-fibrinogen technique in repair of, (1941-
 1942) 94
 recovery of, (1944) 89
 repair of lesions, (1941-2) 94
 sensory, (1944) 90

regeneration of, (1944) 311

suture of, (1944) 17
 coagulated blood plasma, use of, in, (1941-2)
 264

sympathetic, tumours of, (1944) 381

union, experimental work on, (1944) 89

Nervous
 diseases, (1939) 120, (1941-2) 88, (1943) 73
 advances in knowledge of, (1940) 6, 64-74
 anatomy, (1939) 120
 clinical neurology and pathology, (1939) 122
 endocrinology in, (1940) 6
 epilepsy, (1939) 124
 functional treatment of, (1940) 7
 pathology, (1939) 125
 physiology, (1939) 121
 recent work on, (1944) 87
 surgery, (1939) 124
 therapeutics, (1939) 125
 vitamin-B₁ therapy, (1940) 586

Nervous—*continued*
 diseases—*continued*
 vitamin E,
 deficiency and, (1944) 89
 therapy, (1941-2) 426
 energy in aviators, (1943) 141
 factors, shock, in, (1941-2) 386
 impulses, transmission of, (1943) 74
 symptoms,
 adrenaline producing, (1940) 447
 bacterial endocarditis, in, (1941-2) 250
 chicken-pox, in, (1941-2) 189
 diabetes mellitus, in, (1941-2) 206
 extraction of teeth, after, (1941-2) 202
 mumps, in, (1941-2) 309
 sulphonamides cause of, (1939) 176
 whooping-cough, in, (1944) 407

system,
 amyloid disease of, (1943) 116
 anatomy, (1943) 73
 blast injuries and, (1943) 251
 central, in lead poisoning, (1941-2) 282
 diseases of, (1943) 4
 intestinal obstruction and, (1940) 354
 mumps, in, (1940) 412
 opiates, effects of, (1941-2) 338
 physiology, (1943) 74
 vegetative, survey of physiology, (1939) 121
 vitamin E in relation to, (1940) 70

Neuralgia, (1941-2) 314
 atypical, (1941-2) 314
 buccal, (1941-2) 314
 glossopharyngeal and trigeminal, (1939) 445
 migrainous, alcohol treatment of, (1941-2) 307
 superior laryngeal, symptoms and diagnosis,
 (1941-2) 314
 treatment, cobra-venom in, (1940) 300
 trigeminal, (1940) 423
 disseminated sclerosis, in, (1940) 278
 Gasserian ganglion, injection of, (1940) 423
 treatment of, (1939) 445
 division of pain fibres in trigeminal tract,
 (1939) 446
 old tuberculin, (1939) 445
 Sjöquist's operation for, (1939) 124
 vitamin B₁ in, (1940) 423, (1941-2) 314
 liver extract, and, (1940) 423

vesical, (1940) 207

Neurectomy, presacral, child-birth after, (1940) 546

Neutlemmonia of stomach, (1943) 353

Neuritis, (1939) 446
 acute infective polyneuropitis, (1943) 291
 eighth cranial nerve, vitamin B₁ in, (1940) 586
 multiple, (1941-2) 315
 acute infective, (1941-2) 315
 aetiology, (1940) 424, (1944) 312
 arsenical, vitamin B therapy in, (1941-2) 410
 diabetes mellitus, associated with, (1941-2) 206
 dietary deficiencies causing, (1940) 424
 Guillain-Barré syndrome, (1941-2) 315
 haematoporphyrinuria acuta complicated by,
 (1941-2) 239
 hepatic cirrhosis, relation to, (1941-2) 289
 peripheral, (1940) 129
 serum therapy, after, (1939) 446
 sulphonamide application, effect of local, (1944)
 312
 thiamine hydrochloride in, (1940) 424
 vitamin B₁ in, (1940) 129

T A B vaccine causing, (1943) 282

toxic, due to sulphamethylthiazole, (1943) 291

tri-ortho-cresyl cause of, (1939) 13

vitamin B₁ in, (1940) 129
 deficiency cause of, (1939) 14

Neuro-arthritic diathesis, alopecia of peroneal region
 and, (1940) 165

Neuroblastoma
 adrenal medulla, of, (1943) 108
 sympathetecum, radiological appearances and
 treatment, (1943) 354

Neurocirculatory asthenia, (1941-2) 2. *See also* Effort
 syndrome

Neurodermatitis, circumscripta follicularis, (1940)
 345

Neuro-epitheliomas of retina, (1943) 326

CUMULATIVE INDEX

Neurofibroma
 acoustic, (1941-2) 174
 kidney, of, (1943) 260
 larynx, of, (1943) 40
 Neurofibromatosis, (1939) 447, (1943) 291
 bilateral acoustic, (1939) 447
 mouth, involvement of, (1943) 292
 sarcomatous degeneration in, (1943) 291
 Neurogenic
 appendicitis, (1943) 130
 fever, (1944) 346
 Neurology, (1941-2) 88
 advances in, (1944) 87
 recent work in, (1940) 64
 Neuroma, formation, prevention of, (1944) 91
 Neuromuscular diseases, treatment by vitamins E
 and B₆, (1943) 308
 Neuromyelitis optica, (1939) 544
 Neuritis, generalized, (1943) 291
 Neuroses *See also* Psychoneuroses
 experimental, (1943) 66
 forces, in, (1944) 79
 Neurosyphilis, (1939) 447, (1941-2) 315, (1943) 292
 aetiology, (1939) 447
 conjugal, (1941-2) 403
 general paralysis of insane, (1939) 447
 aetiology, (1939) 447
 malarial therapy (cerebral impaludation), (1939)
 447
 T. A. B. vaccine therapy, (1939) 448
 malaria therapy, (1940) 400
 mental disturbances in, (1941-2) 316
 prophylaxis, (1941-2) 316
 spinal, (1939) 448, (1940) 425
 juvenile tabes, (1939) 448
 tabes dorsalis, treatment of, (1939) 448
 treatment, (1941-2) 315
 iodobismutol and saligenin with neoarsphen-
 amine or tryparsamide, (1941-2) 316
 tryparsamide and neocryl, (1941-2) 317
 tryparsamide, nitritoid reactions following,
 (1940) 426
 Neurotrophic origin of alopecia, (1943) 113
 Neutral red excretion test, sprue and pernicious
 anaemia, in, (1944) 378
 New-born
 anaemias, haemolytic, of, (1941-2) 140, (1943) 24,
 119
 asphyxia in, (1941-2) 156, (1943) 138
 atelectasis, massive, in, (1941-2) 290
 dacryocystitis, treatment of, (1941-2) 281
 diarrhoea, infectious, in, (1943) 188
 eventration in, (1941-2) 255
 feeding reflexes in, (1944) 262
 haemorrhage in, (1940) 16
 haemorrhagic diseases of, (1940) 31, 326, (1943)
 230
 vitamin K in, (1940) 591, (1941-2) 50, 427
 antenatal administration of, (1944) 246
 icterus gravis neonatorum, (1941-2) 140, (1943)
 119
 intestinal obstruction, congenital, (1944) 234
 intracranial haemorrhage in, (1940) 16
 maternal nutrition and, (1944) 142-5
 ophthalmia, gonorrhoeal, in, (1943) 179
 platelet count in, (1940) 211
 prothrombin,
 deficiency in, (1940) 31
 time, effect of vitamin K on, (1941-2) 427
 thrush in, (1943) 218
 vitamin K deficiency in, (1940) 591
 Nicamide, nikethamide, official name for, (1940) 127
 Nicotine
 acute poisoning by, (1939) 567
 fatal poisoning in child, (1941-2) 409
 gastric acidity, effect on, (1941-2) 326
 normal and damaged hearts, effect on, (1941-2)
 409
 poisoning, (1940) 557
 angina pectoris, resembling, (1939) 215
 urinary excretion, (1944) 324
 Nicotinic acid, (1941-2) 112
 alcoholic encephalopathy treated with, (1943) 64
 alcoholism treated with, (1940) 157
 asthma treated with, (1944) 155

Nicotinic acid—*continued*
 blood, in, (1940) 115
 deafness, in, (1939) 297
 deficiency,
 encephalopathic syndrome caused by, (1940)
 271
 lesions caused by, (1939) 14
 disseminated sclerosis, in, (1940) 278
 excretion of, (1940) 115
 pellagra, (1939) 18, 149, 462, (1940) 129; (1941-2)
 324
 peripheral vascular system, effect on, (1940)
 452
 pink disease, in, (1939) 475
 porphyrinuria after sulphonamide therapy, (1940)
 129
 senile toxic exhaustion syndromes treated with,
 (1941-2) 82
 sprue treated with, (1940) 542, (1941-2) 399
 sulphonamide, with, (1940) 129
 urine, in, (1940) 115
 Vincent's angina treated with, (1940) 410
 xerostomia due to deficiency, (1941-2) 424
 Night-blindness, (1941-2) 5, (1943) 80, 206, (1944)
 158
 malingering, tests for, (1943) 207
 psycho-physiological origin, (1943) 206
 vitamin A and, (1939) 245, (1940) 128
 vitamin therapy, (1943) 80
 Night flying, (1941-2) 30
 Night-vision, (1944) 158
 aviators, of, (1941-2) 36
 visual capacity, (1941-2) 30
 Nikethamide, (1940) 127, (1941-2) 112
 Nipple
 discharge from, (1941-2) 176
 Paget's disease of, (1940) 231, (1944) 167
 Nitrites, cardiospasm treated with, (1940) 146
 Nitritoid reactions, tryparsamide and, (1940) 426
 Nitro-derivatives, poisoning by, (1940) 562
 Nitrogen
 convulsion therapy, (1940) 59, 496
 metabolism, in mental disorders, (1941-2) 84
 monoxide and oxygen, anaesthesia for operations
 on malignant growth of larynx, (1941-2)
 282
 Nitrogenous constituents of food, (1941-2) 232
 Nitroglycerin, cardiospasm treated with, (1940) 146
 Nitrous oxide
 anaesthesia,
 anaemia in, (1940) 111
 cerebral disturbances, and, (1943) 120
 prevention of, (1944) 136
 ether and convulsions, (1940) 174
 hypoxia, dangers of, (1943) 120
 labour, in, (1940) 19
 sequelae, (1940) 112
 toxic effects, (1940) 111
 cystoscopy, self-administered in, (1939) 330
 oxygen with pentothal sodium anaesthesia, and,
 (1939) 213
 Noctua Noctui, gastric cancer in animals caused by,
 (1940) 240
 Nodes, Heberden's, (1941-2) 243
 Noise, airplane
 aviators, effect on hearing of, (1940) 206, (1941-2)
 36
 Noma *See* Cancerum oris
 Nose
 congenital occlusion,
 nasal choanae, of, (1940) 144
 posterior choanae, of, (1939) 341
 diseases of, (1941-2) 52, 317
 drugs for, (1941-2) 334
 middle turbinate, inflammation of mucosa, cause
 of headache, (1939) 364
 nasopharynx diseases, and, (1939) 449
 chronic hyperplastic rhinitis, glucose treatment
 of, (1939) 449
 folliculitis naris perforans, (1939) 449
 nasal bones fracture, treatment of, (1939) 449
 obstruction, treatment of, (1941-2) 317
 radiography, soft-tissue, (1940) 102
 sinuses *See* Sinuses, nasal accessory
 Notoedus cati, (1941-2) 390

CUMULATIVE INDEX

Novocain
endocervicitis, in, (1940) 289
fibrositis, in, (1940) 7, (1943) 208
herpes zoster treated by injection of, (1941-2) 256
infiltration, Dercum's disease, in, (1939) 188
phlebitis, in, (1940) 582
thrombosis, in, (1943) 375
Novurit in heart failure, (1939) 60
Nuck, hydrocele of canal of, (1941-2) 330
Nucleus pulposus
retropulsion of, (1940) 538
rupture of, (1943) 331
Nupercaine
ocular sensitivity to, (1941-2) 338
spinal anaesthesia, (1944) 136
Nurses, day, (1944) 8
war-time, (1944) 6
Nutrition
industrial workers, of, (1944) 235
maternal, and neonatal haemorrhage, (1940) 16
pregnancy, in, (1944) 22, 142-5
soldiers, of, (1940) 11
sub-optimal, as causal factor in hypertension, (1943) 149
war-time, in, (1943) 214 6
wound healing, and, (1941-2) 13
Nutritional oedema, (1943) 189
Nystagmus
directional preponderance of, in temporal lobe lesions, (1944) 88
miner's, prophylaxis by illumination, (1944) 313
palate, of, (1939) 122

O

Obesity *See also* Adiposity
pathological, after anorexia nervosa, (1944) 141
Obliterative vascular disease, sympathectomy for, (1943) 134
Obstetric shock, (1943) 18, 261
crush syndrome, relation to, (1943) 19
Obstetrics
advances in, (1940) 16 (1941-2) 16, (1943) 15, (1944) 22 *See also* Erythroblastosis foetalis, Labour, Puerperium
gynaecology, and, (1939) 29
endocrinology, (1939) 34
puerperal sepsis, (1939) 31
posterior pituitary extract in, (1941-2) 16
sulphanilamide powder in, (1944) 25
Occipito-posterior position, mechanism and treatment of, (1944) 23
Oclusion
acute embolic, of arteries of extremities, (1944) 83
arterial, peripheral, (1944) 82
Occlusive arterial diseases, treatment, (1943) 133
Occupation
factor in longevity, (1941-2) 379
Weil's disease, and, (1943) 255
Ochronosis, alkaptonuric, (1943) 111
Ocular
changes, alopecia, total, with, (1944) 128
complications,
hyperemesis gravidarum, in, (1943) 17
leontiasis ossea, in, (1940) 225
infections, sulphonamides in, (1941-2) 118
lesions, in rhinosporidiosis, (1940) 512
muscles,
balance, in aviators, (1941-2) 31
myasthenia gravis, in, (1943) 284
pain, retrobulbar injection of proctocaine for, (1941-2) 244
percarine, sensitivity to, (1941-2) 338
Oedema, (1939) 450, (1941-2) 318
advances in treatment of, (1940) 5
aetiology, (1941-2) 318
cardiac, (1943) 1
calcium gluconate in, (1941-2) 254
embarrassment of venous return causing, (1941-2) 318
hereditary, (1939) 450, (1940) 427, (1941-2) 318
a new syndrome, (1943) 293
clinical picture, (1939) 450
hysterical, of hand and forearm, (1940) 426
infantile, vitamin B₁ therapy in, (1939) 450

Oedema—continued

legs, of,
bilateral, (1941-2) 318
persistent, (1941-2) 318
lipodema, (1940) 427
lung, of, associated with menstruation, (1941-2) 318
mercurial diuretics in treatment of, (1940) 5
Milroy-Nonne disease, (1940) 427
nephrotic, treatment of, (1941-2) 313
nutritional, (1943) 189
jejuno-colic fistula causing, (1941-2) 318
salyrgan in treatment of, (1940) 5
Oesophagitis, alcoholic, (1941-2) 134
Oesophagus
achalasia of, (1944) 121
atresia, congenital, (1940) 427, (1941-2) 318
congenital
abnormalities of, (1940) 14
malformations, (1940) 427, (1941-2) 318
congenitally short, peptic ulcer associated with, (1943) 293
diseases, (1939) 450, (1940) 427, (1941-2) 318
acute oesophagitis, thrush cause of, (1939) 450
cancer,
epidermolysis bullosa and, (1944) 225
treatment, (1940) 14
carcinoma, treatment of, (1939) 28
surgical, (1943) 293, (1944) 313
peptic ulcer, clinical picture and treatment of, (1939) 451
simple ulcer, short oesophagus associated with, (1939) 43
familial short, (1940) 428
polyp, multiple, (1944) 313
stenosis, simple non-malignant, (1940) 15
thoracic, removal of, (1940) 14
tumours of, (1944) 313
ulcer, associated with achalasia of cardiac sphincter, (1940) 145
varices, sodium morrhuate in, (1940) 428
Oestradiol, (1943) 98
benzoate, (1943) 97
carcinogenic action of, (1941-2) 183
dysmenorrhoea treated with, (1940) 282
gonadotrophic activity of pituitary, effect on, (1940) 521
involutional melancholia, in, (1940) 488
migraine treated with, (1940) 409
urinary output, effect on, (1940) 522
blood pressure, effect on, (1941-2) 382
climacteric, in, (1939) 280
deoxytocosterone acetate for normal infants, and, (1941-2) 335
dipropionate, climacteric, in, (1940) 248
menopausal symptoms treated by implantation of, (1941-2) 190
tumorigenic action, (1940) 527
Oestrin
breast tissues, effect on, (1940) 21
deafness, in, (1939) 296
diabetes mellitus treated with, (1943) 34
menopausal symptoms treated with, (1941-2) 191
prematurity treated with, (1940) 482
Oestriol, (1943) 97
meno-metrorrhagia, in, (1940) 407
Oestrogen, (1943) 96 *See also* Oestrogens
arthritis treated with, (1940) 201
breast cancer and, (1940) 232
breast tissues, effect on, (1940) 21
cancer tissue, effects on, (1941-2) 183
carcinogenic properties of, (1940) 21
climacteric, in, (1939) 280
deafness, in, (1940) 255
fibromyomas after injections, prevention of, (1941-2) 383
fractures, effect on healing of, (1940) 273
gonorrhoea, in, (1939) 359
gonorrhoeal salpingitis treated with, (1941-2) 228
induction of labour, in, (1940) 374
kraurosis vulvae treated with, (1940) 593
lactation, effect on, (1941-2) 383
laryngeal papilloma treated with, (1940) 376, (1943) 43
leucoplakia of tongue, in, (1940) 410

CUMULATIVE INDEX

Oestrogen—continued

- menorrhagia, in, (1939) 430
 - new derivatives, (1941-2) 335
 - otosclerosis, in, (1940) 255
 - ozæna treated with, (1940) 429
 - pharmacological actions, (1943) 96
 - pituitary and pancreas, action on, (1941-2) 382
 - pregnancy toxæmias, in, (1940) 18
 - prolonged administration, effect of, (1940) 521
 - prophylactic implantation of, (1943) 20, 164
 - replacement therapy, in climacteric, (1943) 334
 - synergism with pituitary gonadotropins, (1941-2) 384
 - synthetic, uses of, (1939) 34, 110
 - therapeutic uses, (1943) 96
 - union of fractures, role in, (1941-2) 211
 - uterine bleeding, in, (1941-2) 21
 - vaginitis,
 - gonococcal, treated with, (1940) 594
 - senile, treated with, (1941-2) 429
 - vulvo-vaginitis treated with, (1940) 320, (1943) 91
- ## Oestrogenic substances
- carcinogenic action of, (1941-2) 183
 - pituitary gland, anterior lobe, effect on, (1943) 333
- ## Oestrogens, (1944) 48 See also Oestrogen
- acromegaly treated with, (1944) 122
 - assay, (1944) 49
 - atrophic rhinitis treated with, (1944) 314
 - cyclical therapy, (1944) 370
 - dysmenorrhœa, spasmodic, treated with, (1944) 26, 211
 - implantation, for menopausal symptoms, (1944) 27
 - leucoplakia treated with, (1944) 27
 - menopausal symptoms treated with, (1944) 27
 - otosclerosis treated with, (1944) 53
 - pruritus, senile, treated with, (1944) 337
 - vulvovaginitis treated with, (1944) 406
- ## Oestrone (1940) 132 (1943) 97
- benzoate, (1943) 98
 - breast, action on, (1939) 264
 - galactorrhœa, in, (1939) 220
 - diabetes mellitus during menopause treated with, (1941-2) 191
 - mammary tumours produced by, (1940) 231
 - menopausal symptoms treated by implantation of, (1941-2) 190
 - menopausal syndrome treated by implantation of, (1943) 175
- ## Oestrous cycle, in cats, effect of light on, (1941-2) 384
- ## *Onchium albicans*, (1941-2) 285
- ## Oil
- aspiration (lipid) pneumonia, (1941-2) 177
 - local anaesthetics in, (1940) 349
 - pine, aromatic, of, (1943) 96
 - sulphonated, as detergent in dermatitis venenata, (1941-2) 203
 - wintergreen, of, fatal poisoning by, (1941-2) 409
- ## Oiled floors and oiled linen, (1943) 53
- ## Old age See also Longevity Senescence, Senility
- appendectomy in, (1940) 191
 - appendicitis in, (1941-2) 148, (1943) 129
 - bronchitis, chronic, in, (1944) 170
 - care of aged poor, (1941-2) 379
 - centenarians, rarity of, (1940) 518
 - cholecystotomy in, (1940) 307
 - convalescence in, (1940) 518
 - diseases in, (1940) 519, (1941-2) 380
 - emergency operations in, (1943) 12
 - exercise, dangers of, (1943) 331
 - fibrositis in, (1941-2) 229
 - gastro-intestinal symptoms in, (1941-2) 380
 - hernia, strangulated, in, (1940) 340
 - hermectomy in, (1940) 341
 - liver function tests in, (1944) 286
 - normal, (1941-2) 379, (1943) 331
 - operative risks in, (1941-2) 380
 - osteoporosis of spine in, (1941-2) 381
 - pathological, (1941-2) 380, (1943) 332
 - physiological changes of, (1944) 367
 - prophylactic effect of pneumococcus polysaccharide in, (1941-2) 355
 - rheumatic fever, acute, in, (1941-2) 380
 - rheumatism in, (1941-2) 229, 381

Old age—continued

- scurvy in, (1941-2) 425
 - surgery, in, (1941-2) 380
 - syphilitic infection, incidence of, (1941-2) 380
 - tuberculosis, pulmonary, in, (1944) 291
 - vitamin treatment, effect of, (1943) 332
- ## Olecranon, fracture of, (1941-2) 14
- ## Olfactory tests, diagnosis of supratentorial lesions by, (1944) 165
- ## Oligoseptic treatment, ocular infections, in, (1940) 445
- ## Oliguria, blood transfusion causing, (1943) 30
- ## Omentum
- great, torsion, (1941-2) 125
 - sarcoma of, (1941-2) 329
- ## Onycholysis, (1940) 418
- ## Onychorrhexis, (1941-2) 311, (1944) 308
- ## Operating room, sterilization of air in, (1940) 150
- ## Operations
- aged, in, (1941-2) 380
 - pulmonary complications See Lung, post-operative complications
 - pyrexia following, (1940) 502
- ## Ophthalmia
- gonococcal, sulphanilamide therapy, (1940) 251
 - gonorrhœal, (1943) 178
 - epidemic, in children, (1943) 178
 - neonatorum,
 - effect of control methods on incidence, (1939) 128
 - sulphanilamide in, (1939) 291
 - sulphapyridine in, (1941-2) 196
 - sulphonamides in, (1943) 179
 - nodosa, aetiology of, (1941-2) 196
- ## Ophthalmic strain, industry, in, (1944) 259
- ## Ophthalmic surgery, (1943) 81
- ## Ophthalmology, (1943) 79 See also Eye
- chemotherapy by iontophoresis in, (1944) 220
 - survey of, (1939) 128
- ## Ophthalmoplegia
- chronic progressive, (1941-2) 319
 - exophthalmic, (1941-2) 319
- ## Ophthalmoscopy, clinical medicine, in, (1944) 232
- ## Opiates, effects on nervous system, (1941-2) 338
- ## Opium, pre-anaesthetic sedative for children, as, (1941-2) 143
- ## Opsonic index, cerebrospinal fever, in, (1941-2) 186
- ## Optic
- atrophy,
 - primary, associated with myoclonus epilepsy, (1940) 295
 - syphilitic primary, tryparsamide in, (1940) 210
 - treatment of, (1939) 244
 - tryparsamide therapy, (1941-2) 162
 - chiasma, symptom-complexes associated with, (1941-2) 174
 - nerve tumours, primary, (1943) 147
 - thalamus,
 - hemiplegia and, (1940) 64
 - lesions,
 - cerebral cortex and, (1940) 64
 - dementia resulting from, (1940) 64
 - mental degeneration and, (1939) 122, (1940) 64
 - monkeys, in, (1940) 65

Orbit

- dermoid cyst of, (1943) 184
- rhabdomyosarcoma of, (1943) 147

Orchidectomy

- carcinoma of prostate treated by, (1943) 313
- compensatory testicular hypertrophy after uni-lateral, (1940) 550

Oriental sore

- treatment, (1944) 284
 - antimony injections, (1944) 284
 - berberine sulphate, (1940) 136
 - curettage, (1944) 284
 - irradiation, (1944) 284
 - stibophen in, (1940) 136
 - sulphonamides, (1944) 284
 - powdered, (1940) 378
- Oro-maxillary fistulae, (1944) 304
- Orthoptic treatment, squint, of, (1944) 381
- Os calcis, fractures of, (1939) 315
- treatment by triple arthrodesis, (1944) 206

CUMULATIVE INDEX

- Oscillating bed, occlusive arterial disease treated by, (1940) 194
- Ossification, sternomastoid, of, (1940) 413
- Osteitis
- condensans of ilium, (1939) 253
 - deformans,
 - adrenal cortical preparations in, (1940) 225
 - fluorides in relation to, (1939) 253
 - mono-osteitic type, (1941-2) 172
 - pathogenesis, (1940) 225
 - protruded intervertebral disk associated with, (1941-2) 396
 - treatment, (1940) 225
 - fibrosa, (1943) 160
 - cystica, parathyroids, relation to, (1939) 26
 - tuberculosis multiplex cystoides, (1943) 160
- Osteoarthritis
- aspiration of joint effusions, in, (1940) 200
 - complication of fracture of the ankle, as, (1941-2) 211
 - gold therapy and diet in, (1939) 278
 - spine, of, (1943) 137
 - physiotherapy, (1944) 154
 - treatment, surgical, (1941-2) 153
- Osteoarthropathy
- hypertrophic, (1944) 276
 - pelvic, of pregnancy, (1940) 482
 - pulmonary, (1941-2) 274, (1944) 276
- Osteochondritis
- apophyses of acromion, of, (1940) 296
 - dissecans, (1940) 360, (1943) 256
 - hip, of, (1940) 360
 - loose bodies in, (1940) 360
 - still-born, in, (1943) 356
 - vertebralis, (1940) 539
- Osteoclastoma, treatment by irradiation, (1941-2) 172
- Osteogenic sarcoma, (1940) 227, (1943) 161
- Osteoma, maxillary sinus, of, (1938) 184
- Osteomalacia, (1939) 546
- cataract associated with, (1941-2) 186
 - columnae, (1940) 540
 - spine, of, (1940) 540
 - vitamin D and, (1940) 130, 589
- Osteomyelitis
- acute, (1939) 253
 - recurrent infection, (1940) 226
 - spine, of, treatment, (1941-2) 397
 - superior maxilla, of, (1939) 253
 - treatment, (1939) 253
 - chemotherapy, (1941-2) 172
 - maggot therapy, (1939) 254
 - sulphathiazole, (1940) 134, (1941-2) 49
 - toxoid, (1940) 226
 - ulceron, (1939) 254
 - staphylococcus, (1941-2) 397
 - sulphathiazole in treatment, (1941-2) 49
- Osteopathia condensans disseminata, (1941-2) 171
- Osteopetrosis, (1941-2) 171; (1943) 159
- Osteophytes, hands, of, (1941-2) 243
- Osteopoiikilosis, (1941-2) 171
- Osteoporosis
- aetiology, (1940) 225
 - gastro-intestinal symptoms, (1940) 225
 - hyperparathyroidism, in, (1941-2) 322
 - post-traumatic, treatment of, (1941-2) 173
 - spine, of, senile, (1941-2) 381
- Osteosclerosis
- fluorine causing, (1940) 560
 - fragilis generalisata, (1941-2) 171, (1943) 159
- Otitic hydrocephalus, (1940) 66, 345
- Otitis media, (1939) 323
- acute,
 - complications, (1941-2) 216
 - convulsions, (1941-2) 216
 - treatment,
 - chemotherapy, (1941-2) 57
 - sulphanilamide, (1941-2) 216
 - sulphonamide, (1944) 219
 - aero-,
 - acute, (1940) 49
 - chronic, (1940) 49
 - helium-oxygen therapy in, (1941-2) 182
 - 'blue drum' or idiopathic haemorrhagic tympanum, (1943) 198
- Otitis media—continued
- cholesteatomas, (1939) 324
 - complications,
 - facial paralysis, (1944) 219
 - intracranial, (1943) 199
 - meningitis, (1941-2) 217
 - petrositis, (1943) 199
 - dysentery, after, (1939) 323
 - sedimentation rate, (1939) 323
 - sulphanilamide in, (1939) 323
 - sulphonamides in, (1940) 284, (1941-2) 118
 - suppurative, (1944) 219
 - urea and caroid, (1939) 324
- Otogenic cerebellar abscess, (1943) 162
- Otology, (1939) 86, 322, (1941-2) 52
- chemotherapy in, (1941-2) 56
- Otomycosis, metacresyl acetate and thymol in, (1940) 284
- Otoneurological diagnosis of intracranial tumours, (1939) 94
- Nylen's observations, (1939) 94
- Otorhinolaryngology, (1939) 86
- otology, (1939) 86
 - pharynx and larynx, (1939) 90
 - rhinology, (1939) 90
- Otorrhoea, aigryol in, (1940) 284
- Otosclerosis, (1939) 87
- diagnosis of, (1941-2) 201
 - halisteresis and, (1943) 181
 - hormone therapy, (1944) 53
 - Lempert's operation, (1939) 87
 - methylene blue and sodium ricinoleate in, (1940) 255
 - oestrogenic substances in, (1940) 255
 - treatment, (1940) 255
 - preventive and palliative methods, (1944) 194
 - surgical methods, (1944) 194
- Quabain
- cardiac arrhythmias treated with, (1944) 321
 - heart failure treated with, (1941-2) 254
- Ovarian
- extract in haemophilia, (1939) 362
 - hormones, (1941-2) 382
 - cervix, influence on, (1940) 22
 - follicle-stimulating, (1941-2) 382
 - pituitary gland, anterior lobe, effect on, (1943) 333
- infantilism, (1944) 208
- pregnancy, (1940) 481
- Ovary
- carcinoma,
 - metastatic ureteral obstruction resulting from, (1941-2) 278
 - primary signet-ring cell, (1941-2) 319
 - treatment, (1941-2) 320
 - combined prolan and the pituitary synergist, effect of, on, (1941-2) 22
 - dermoid cyst,
 - malignant, (1941-2) 320
 - traumatic rupture of, (1941-2) 319
 - diseases and tumours, (1939) 451, (1940) 428, (1941-2) 319, (1944) 313
 - adrenal cortical, masculinization associated with, (1940) 156
 - arrhenoblastoma (masculinizing), (1939) 452, (1943) 294
 - carcinoma, signet-ring cell, (1941-2) 319
 - clinical types, (1941-2) 319
 - differential diagnosis, (1939) 451
 - dysgerminoma (seminoma ovarii), (1939) 451, (1940) 428
 - pseudo-hermaphrodite, in, (1943) 294
 - endometriosis, malignant, (1939) 329
 - fibroma, hydrothorax associated with, (1944) 314
 - ganglioneuroma, (1939) 452
 - granulosa-celled and theca-celled (feminizing tumour), (1939) 451; (1940) 428; (1941-2) 320, (1943) 294
 - gynandroblastoma, (1944) 314
 - hypernephroma, (1940) 429
 - incidence, symptomatology and prognosis, tumours, (1941-2) 319
 - malignancy and section, (1941-2) 319
 - masculinizing, (1940) 156

CUMULATIVE INDEX

Ovary—continued

- diseases—continued
 masculinoblastoma, (1939) 452
 melanoma, primary, (1943) 295
 mesonephroma, (1943) 295
 teratomas, (1941-2) 320
 thecoma, (1944) 314
 thyroid, (1943) 294
 treatment, elderly women, in, (1944) 314
 gonadotropins, effect on, (1943) 20
 headache due to functional insufficiency, (1940) 329
 Meigs's syndrome, (1944) 314
 Overlying, infant mortality, as cause of, (1939) 38
 Ovulation
 absence of, (1944) 26
 basal body temperature at time of, (1944) 26
 biochemical assays, (1944) 26
 biopotentials, (1944) 26
 electrical determination of, (1944) 379
 endometrial biopsy, (1944) 26
 intermenstrual bleeding, (1944) 26
 methods for determining time of, (1944) 25
 mittelschmerz and, (1944) 26
 pain due to, simulating appendicitis, (1940) 190
 sterility due to absence of, (1944) 26
 vaginal smears, (1944) 26
 Oxycephaly, (1939) 453, (1943) 295
 surgical treatment, (1939) 453
 Oxygen
 haemoptysis, injection in, (1939) 362
 helium-oxygen mixture, effect of, on voice, (1941-1942) 335
 migraine, inhalation of, (1939) 433
 supply, during and after anaesthesia, (1940) 110
 tension, low, effect upon experimental tuberculosis, (1944) 392
 therapy,
 anuria, in, (1943) 174
 asphyxia in new-born, in, (1941-2) 156
 blackwater fever, in, (1939) 242
 delirium tremens, in, (1940) 173
 improvements in, (1940) 6
 migraine, in, (1940) 409, (1941-2) 307
 pneumonia, in, (1940) 473
 sedative effect of, (1940) 173
 shock, in, (1944) 371
 X-ray diagnosis, in, (1940) 538
 want in aviators, (1941-2) 32, (1943) 6, 139
 Oxylan, (1943) 94
 Oxytic substance, presence in blood of pregnant women, (1941-2) 278
 Oxytocic drugs, poisoning by, (1940) 559
 Oxyuriasis, (1941-2) 311
 appendicitis caused by, (1943) 129
 Cellophane swab test, (1944) 308
 children, in, (1941-2) 311, (1944) 308
 incidence, (1941-2) 311, (1944) 308
 N I H swab examination, (1941-2) 312
 pathogeny, (1941-2) 312
 symptoms, (1941-2) 312, (1944) 308
 treatment, (1941-2) 311
 diphenan in, (1943) 94
 fatal phenothiazine poisoning, (1944) 309
 gentian violet in, (1940) 419, (1944) 309
 phenothiazine in, (1941-2) 122, (1943) 287
Ovaris vermicularis, (1941-2) 311
 appendix, in, (1941-2) 149
 Ozaena, (1939) 453
 treatment,
 oestrogens, (1940) 429, (1944) 314
 progesterone, (1939) 453
 surgical, (1939) 453

P

- Pachydermiosis, achropachyderma with, (1943) 105
 Paediatrics, (1941-2) 4, 48
 Paget's disease
 bone, of, mono-ostietic type, (1941-2) 172
 nipple, of, (1944) 167
 skin, of, (1940) 231

Pain, (1939) 454

- abolition of, (1939) 454
 anatomical basis, (1939) 454
 anginal, (1940) 182, (1941-2) 144
 back,
 low, radiological diagnosis, (1943) 142
 simulating visceral disease, (1943) 142
 cobra-venom for intractable, (1940) 429, (1941-2) 419
 coronary thrombosis, in, (1941-2) 145
 hands and feet in acromegaly, in, (1941-2) 129
 intermenstrual, (1941-2) 21
 left-sided, in diseases of biliary tract, (1943) 219
 ocular, retrobulbar injection of proctocaine for, (1941-2) 244
 pethidine hydrochloride for relief of, (1944) 326
 pleural, procaine for relief of, (1940) 473
 post-operative, demerol in treatment of, (1944) 321
 prostigmin methylsulphate and morphine for relief of, (1941-2) 338
 sciatic, (1943) 4
 shoulder, associated with myocardial infection, (1941-2) 249
 survey of, (1939) 19
 thresholds for, measurement, (1941-2) 320
 visceral, associated with dextrocardia, (1941-2) 246

Palate

- cleft, and hare-lip, (1939) 454
 dental plate facilitating feeding, (1939) 454
 myoclonus, (1940) 411
 nystagmus of, (1939) 122
 Palm oil, red, (1941-2) 308
 Pamaquin, (1940) 76, 127, (1941-2) 112
 malaria treated with, (1940) 136
p-aminobenzenesulphonacetamide, (1943) 99
p-aminobenzoic acid, control of sulphathiazole therapy by, (1941-2) 344

Pancoast's tumour of lung, (1941-2) 294

Pancreas

- abnormalities, developmental, (1940) 430
 action of oestrogens on, (1941-2) 382
 adenoma, hypoglycaemia in, (1943) 245
 annular, (1940) 430
 calculi, (1941-2) 321
 aetiology of calcification of parenchyma, (1943) 296
 operative treatment, (1943) 296
 radiological investigation, (1943) 296
 carcinoma, (1940) 432, (1943) 296, (1944) 254
 of head of, (1941-2) 321
 treatment,
 operative, (1943) 297
 surgical, (1944) 315
 cyst, (1941-2) 321, (1944) 315
 disease, (1939) 455, (1940) 430-2, (1941-2) 321, (1944) 20, 315
 acute necrosis, (1939) 455
 adenocarcinoma, (1939) 456
 adenoma, (1939) 456
 arrhythmia, associated with, (1939) 455
 calculi, diagnosis of, (1939) 456
 congenital cystic disease, (1939) 456
 secretion test in diagnosis of, (1941-2) 322
 serum amylase test, (1944) 20
 epithelioma, (1940) 432
 fibrocystic disease, (1944) 315
 fistulae, (1944) 315
 inflammatory conditions, (1941-2) 321
 lipocae, (1940) 430
 necrosis, acute pancreatic, (1940) 431
 physiology, (1940) 430
 secretion, (1944) 315
 tuberculosis, (1940) 431
 tumours, (1940) 431, (1941-2) 321; (1944) 315
 diagnosis, (1940) 431
 Pancreatic
 duct relation to biliary duct, (1939) 346
 extracts,
 epilepsy treated with, (1940) 294
 insulin-free, (1940) 430
 new, (1944) 324

CUMULATIVE INDEX

- Pancreatic**—*continued*
 extracts—*continued*
 peripheral arterial disease treated with, (1944) 324
 uterine occlusion treated with, (1940) 368
 necrosis, acute, (1940) 431
- Pancreatitis**,
 acute,
 haemorrhagic, diabetes mellitus complicating,
 (1941-2) 321
 interstitial, (1940) 431
 serum amylase test, (1943) 296
 surgical aspects, and treatment, (1943) 296
 petrifying, (1943) 296
 serum amylase test, (1944) 20
- Panniculitis**, (1939) 457
- relapsing febrile nodular non-suppurative, (1943) 208
- Pantocaine** (decicam), (1941-2) 113
- local anaesthesia, in, (1939) 210
- Pantothenate**, (1944) 368
- Pantothenic acid**, riboflavin deficiency and, (1941-2) 424
- Pantoylaurine**, haemolytic streptococci, influence on, (1944) 368
- Papaverine**
 benzyl- β -dimethylamino- α -phenyl- α -ethylpropionate hydrochloride compared with, (1941-2) 333
 colic, in, (1939) 165
 spasm, for, (1939) 165
- Papilla**, 'snow-capped', (1941-2) 312
- Papilloedema**, morbid anatomy of, (1939) 458
- Papilloma**
 larynx, of, (1943) 42
 oestrogenic therapy, (1940) 376
 malignant, in diverticulum of bladder, (1943) 145
 vesical, (1944) 156
- Parachute descents**, (1941-2) 33
- portable oxygen set, (1941-2) 33
- Para-dichlorobenzene**, cataract caused by inhalation of, (1940) 243
- Paraffin**
 liquid,
 absorption into tissues, (1941-2) 337
 pack in treatment of pulmonary tuberculosis, (1941-2) 293
- Paraffinoma**, result of liquid paraffin treatment, as, (1941-2) 330
- Paraffin-pack apicolysis**, (1940) 392
- Paraldehyde**
 addiction, visual hallucinations in, (1944) 208
 analgesia in labour, (1941-2) 280
 intramuscular injection of, in obstetrics, (1943) 261
 poisoning, acute, (1943) 363
 prolonged narcosis by dial and, (1940) 418
- Paralysis**
 agitans, (1939) 458
 Bulgarian belladonna root treatment, (1939) 458
 treatment,
 quinine, (1941-2) 322
 vitamin B₁, (1944) 316
 vitamin B₆, (1941-2) 5, 322
 diaphragmatic, in infancy, (1943) 290
 hemi-diaphragmatic, in pulmonary tuberculosis, (1941-2) 292
 hemiplegia,
 anosognosia and autotopnosia, with, (1943) 75, 241
 disturbances of body scheme, with, (1943) 75
 herpes zoster causing, (1941-2) 256
 hysterical, in soldier, (1941-2) 363
 muscular, electrotherapy, (1943) 77
 Parrot's pseudo-, (1941-2) 404
 periodic,
 familial, associated with hyperthyroidism, (1943) 298
 myasthenia gravis, relation to, (1940) 69
 plasma potassium in, (1940) 114
 potassium chloride in, (1940) 68
 sleep, (1943) 287
 tick, (1944) 154
 transient, postural hypotension causing, (1940) 217
- Paranoia**, clinical picture, (1941-2) 365
- Parapertussis**, (1943) 180
- Paraplegia**, measles complicated by, (1941-2) 302
- Parapsoriasis**
 clinical types, (1944) 316
 histological changes, (1944) 316
- Parasites**
 intestinal, treatment by phenothiazine, (1941-2) 122
 skin diseases due to, (1941-2) 390
- Parasympathomimetic drugs**, (1941-2) 346
- Parathormone** in lead poisoning, (1939) 400
- Parathormone-shock** treatment, tetany, post-operative, in, (1940) 433
- Parathyroid**
 extract, thrombocytopenic purpura treated with, (1941-2) 241
 gland, (1944) 46
 diseases, (1939) 459, (1940) 432-4, (1941-2) 322, (1943) 298
 hyperparathyroidism, (1939) 460
 Hamilton and Highman's test in diagnosis, (1939) 460
 morbid anatomy renal changes, (1939) 460
 hypoparathyroidism, (1939) 459
 bone graft implantation, (1939) 460
 calcium lactate, (1939) 460
 dihydroxyachysterol in treatment, (1939) 459
 physiology, (1944) 316
 removal, mental condition following, (1940) 54
 tetany and, (1944) 316
 psychosis complicating, (1941-2) 322
 hormone, bones, action on, (1944) 316
- Paratyphoid fever**
 aetiology, (1944) 223
 rain-water, dangers of, (1944) 223
- Paratyphoid B fever**, (1944) 38
- aetiology, (1944) 223
 treatment, sulphaguanidine, failure of, (1944) 224
 water supply and infection, (1944) 224
- Paredrine**
 bradycardia, in, (1939) 223
 eye examination, in, (1939) 337
 hypotension, effect on, (1939) 250, (1940) 176
 intravenous drip administration, (1941-2) 346
 pressor effect, (1940) 450
 shock, in, (1941-2) 389
 sodium amylal anaesthesia, effect on, (1940) 178
 spinal anaesthesia, in, (1940) 176
- Paraldrinol**
 effect on circulation, (1941-2) 388
 experimentally produced shock, in, (1941-2) 388
 shock and collapse, in, (1940) 529
- Paresis**, mild, 'lowering the arm' sign, in, (1940) 412
- Parietal foramina**, congenital bilateral, (1940) 224
- Parnaud's oculo-glandular syndrome**, (1941-2) 109
- Parkinsonism**
 arteriosclerotic, treatment, (1944) 166
 encephalitis epidemica causing, (1941-2) 220
 treatment, (1944) 221
 post-encephalitic, (1939) 327
 benzedrine sulphate in, (1940) 287
 syntropan, in, (1941-2) 220
- Parkinson's syndrome**, treatment, (1944) 166
- Paronychia**, gentian violet and brilliant green in, (1940) 304
- Parotid gland**
 diseases, (1939) 461; (1940) 434, (1941-2) 323
 sialography in diagnosis, (1939) 461
 inflammation, (1944) 317
 mixed tumours, treatment of, (1943) 299
 total parotidectomy for, (1941-2) 323
 premenstrual salivary syndrome, (1940) 434
- Parotidectomy**, total, (1941-2) 323
- Parotitis**
 acute, (1944) 317
 post-operative, treatment with radium, (1943) 299
 secondary, acute, Lugol's solution in, (1940) 434
 suppurative, acute, X-ray therapy, (1940) 434
 surgical, (1944) 317
- Parrot's pseudo-paralysis**, (1941-2) 404
- Passive vascular exercises**, (1940) 196
- Pasteurella**
 pseudotuberculosis rodentium, human infection with, (1943) 223
 tularensis, (1941-2) 415
- Patella**, habitual dislocation of, (1939) 392

CUMULATIVE INDEX

- Patent ductus arteriosus, (1941-2) 2
 Paterson's syndrome, (1939) 43
 Pathology, chemical, (1940) 113
 Paul-Bunnell test, glandular fever, in, (1941-2) 235, (1943) 222
 Pavex machine, treatment of compression injuries, in, (1941-2) 9
 Pectin-agar, infantile diarrhoea, in, (1940) 270
 Pectoralis major muscle, fixation of, malignant tumours of breast in, (1941-2) 176
 Pediatrics, (1941-2) 4, 48
 Pediculosis
 temperatures lethal to lice, (1940) 531
 treatment of, (1941-2) 391
 Pellagra, (1939) 461, (1941-2) 324
 aetiology, (1940) 435, (1941-2) 324
 alcoholism, chronic, and, (1941-2) 324
 amino-acids in treatment, (1939) 463
 biochemical changes in blood, (1939) 461
 cheilitis in, (1940) 435
 history, (1943) 300
 liver extract therapy, (1939) 463
 morbid anatomy and pathology, (1941-2) 324
 nicotinic acid treatment, (1939) 18, 149, 462
 pellagra-like condition associated with diabetes mellitus, (1941-2) 206
 peripheral nerves in, (1941-2) 324
 'sore mouth' and, (1941-2) 308
 synthetic nicotinamide, (1939) 463
 treatment,
 nicotinic acid, (1940) 129
 quinolinic acid, (1940) 436
 vitamin B, (1941-2) 324
 vitamin C, (1941-2) 324
 Pelvic infection, iontophoresis in, (1941-2) 217
 Pelvis, osteoarthropathy of pregnancy, (1940) 482
 Pemphigoid lesions in leprosy, (1943) 264
 Pemphigus and pemphigoids, (1939) 463, (1940) 436, (1941-2) 324, (1944) 317
 acute,
 aetiology, (1940) 436
 complicating chicken-pox, (1941-2) 189
 history and nomenclature, (1944) 318
 neonatorum, carrier of, (1941-2) 325
 sulphapyridine in, (1940) 436
 ocular, (1939) 464
 solitarius cicatricans, (1941-2) 325
 vulgaris, (1939) 463
 calciferol in, (1939) 463
 dihydrocalcysterol in, (1941-2) 324
 germann, (1939) 464
 serum from bullae, (1939) 464
 Penicillin, (1941-2) 6, 119, (1943) 5, (1944) 13
 action of, (1941-2) 119
 antiseptic snuff, as, (1941-2) 331
 burns, infected, treated with, (1944) 173
 cavernous sinus thrombosis treated with, (1943) 14, (1944) 13
 chemotherapeutic properties of, (1941-2) 338
 effects in different cases, (1944) 324
 gonorrhoea treated with, (1944) 108
 pharmacology of, (1944) 325
 recent work on, (1944) 115
 resistance, natural and acquired, to, (1944) 325
 septic conditions, use in, (1944) 326
 staphylococcal infections treated with, (1944) 368
 Staphylococcus aureus, effect on, (1944) 325
 therapeutic trials, (1941-2) 120
 toxicity and bacteriostatic effects, (1943) 302, (1944) 325
Penicillium notatum, (1941-2) 6, 119
 Penis
 carcinoma, radium therapy, (1941-2) 325
 corpus cavernosum, as transfusion site, (1943) 31
 diseases, (1941-2) 325
 elephantiasis,
 lymphopathia venereum, in, (1940) 398
 surgical treatment, (1941-2) 325
 plastic induration of, (1940) 437
 serotum, and, diseases, (1939) 465
 carcinoma, treatment of, (1939) 465
 congenital absence of, (1939) 586
 priapism, (1939) 465
 thrombophlebitis, (1939) 465
 underdeveloped. *See* Hormone therapy
 Pentnucleotide, agranulocytosis, in, (1939) 194
 Pentothal, (1939) 163
 labour, in, (1939) 397
 Pentothal acid
 basal narcotic, as, (1939) 211
 labour, use in, (1940) 375
 sodium, (1940) 177
 anaesthesia,
 intermittent administration, (1944) 137
 uses and dangers, (1944) 137
 encephalography, for, (1940) 178
 fractures, in reduction of, (1940) 177
 peroral endoscopy, in, (1943) 121
 respiratory depression caused by, (1940) 177
 thrombosis caused by, (1939) 211
 Peptic ulcer, (1939) 466, (1941-2) 326; (1943) 11, 300, (1944) 318-20
 aetiology, (1939) 466, (1940) 437, (1941-2) 326, (1944) 318
 age influence, (1941-2) 326
 alkali poisoning in, (1941-2) 135
 aluminium hydroxide, colloidal, in treatment, (1939) 167, 468
 antacids in treatment of, (1939) 22, 167
 autonomic system, role of, (1944) 318
 aviators, in, (1941-2) 160
 belladonna in, (1939) 167
 central nervous system complications, (1939) 468
 childhood, in, (1941-2) 326
 chronic, site of, (1940) 438
 clinical picture, (1940) 438, (1941-2) 326
 complications, treatment of, (1941-2) 328
 diabetes associated with, (1939) 301
 diagnosis, (1944) 319
 phenolphthalein test in, (1939) 467
 differential diagnosis, benign or malignant character, (1944) 319
 digestive disorders in soldiers, (1943) 2, 198
 emotions, influence of, (1944) 31
 experimentally produced ulcers, (1939) 466
 family history of, (1940) 26
 gastric acidity, (1940) 437
 factors affecting, (1939) 466
 haematemesis caused by, (1943) 300
 haemorrhage in, (1943) 45
 pernicious, (1940) 438
 histamine factor, (1941-2) 326
 hypothalamus, role of, (1944) 318
 ileum opposite Meckel's diverticulum, perforation of, (1943) 102
 infancy and childhood, incidence in, (1943) 300
 melana, (1940) 439
 multiple perforating ulcers, (1939) 470
 oesophagus, of, (1943) 293
 pathology and morbid anatomy, (1940) 438, (1941-2) 326
 perforation of, (1940) 437
 after-history, (1944) 319
 diagnosis, (1940) 438
 simultaneous, (1941-2) 326
 psychological factors in, (1939) 15, 466; (1944) 318
 renal calculi and alkaline therapy, (1940) 442
 smoking, relation to, (1941-2) 326
 soldiers, in, (1940) 25, (1941-2) 214, (1943) 2, 198
 stomach and duodenum, (1941-2) 326
 treatment, (1940) 439-42, (1941-2) 326
 alkalis, (1940) 439
 renal calculus after, (1940) 442
 aluminium hydroxide, (1941-2) 327, (1944) 32
 colloidal, (1940) 439
 intra-gastric drip method, (1940) 440
 aluminium phosphate gel, (1941-2) 327
 antacids, (1940) 439
 bleeding ulcers, of, (1941-2) 328
 colloidal aluminium hydroxide, (1941-2) 327
 complications, of, (1941-2) 328
 enterogastrone and urogastone, (1943) 301
 Forces, in, (1944) 319
 gastric resection and acidity, (1941-2) 327
 histaminase, (1940) 441
 insulin, (1939) 469

CUMULATIVE INDEX

Peptic ulcer—continued

treatment—continued

- magnesium trisilicate, (1939) 469, (1940) 441, (1941–2) 328
- Meulengracht regime, (1941–2) 328; (1943) 300
- partial gastrectomy, (1940–2) 326
- posterior pituitary powder insufflation, (1940) 441
- progynon, injection of, (1940) 441
- surgical, (1939) 27, 469, (1940) 442
- results of, (1944) 319
- syntrogeol, (1941–2) 327
- vitamin A (avoleum), (1941–2) 327
- inefficacy of, (1944) 319
- vitamin B deficiency, relation to, (1939) 466
- Peptone, inhibition of action of sulphanilamide by, (1940) 458
- Per-abrodil, poisoning by, (1940) 503
- Perandren, blood pressure, effect on, (1941–2) 382
- Percaime, ocular sensitivity to, (1941–2) 338
- Percorten, (1943) 94
- Periarthritis nodosa, (1941–2) 151
- abdominal symptoms, (1940) 194
- aetiology and clinical picture, (1939) 224
- anaphylaxis and, (1944) 151
- asthma and, (1940) 202
- clinical picture, (1940) 193
- diagnosis by sigmoidoscopy (1943) 132
- histological appearances, (1943) 132
- renal insufficiency, effect of, (1944) 150
- surgical significance of symptoms, (1943) 132
- Periarthritis, suppurative, *Bacillus supestifer* infection in, (1943) 135
- Pericardiectomy for constrictive pericarditis, (1939) 60
- Pericarditis
 - constrictive, (1943) 234
 - chronic, with calcification, (1940) 332
 - treatment of, (1939) 60
 - rheumatic, salicylate therapy, (1941–2) 248
 - suppurative, pericardostomy in, (1943) 235
 - treatment, sulphathiazole in, (1941–2) 49
- Pericardium
 - adherent, radiocardiography (or, (1939) 58
 - diseases, (1941–2) 248, (1943) 234
 - foreign bodies, (1940) 333
- Pericardostomy, suppurative pericarditis treated with, (1943) 235
- Perineal anaesthesia, in labour, (1941–2) 280
- Perinephric abscess, (1943) 258
- Periodic catatonias, thyroxine treatment of, (1939) 119
- Periodontal disease, vitamin A in relation to, (1940) 128
- Peripheral
 - arterial
 - diseases, pancreatic extract in treatment, (1944) 324
 - occlusion, (1944) 82
 - circulation, (1944) 81
 - nerves, (1943) 74
 - polyneuritis, ankylostomiasis, associated with, (1939) 218
 - vascular system,
 - cigarette smoking and deep breathing, effects of, (1940) 196
 - nicotinic acid, effects of, (1940) 452
 - passive vascular exercises in, (1940) 196
 - treatment, prostigmin in, (1940) 196
- Perisymphathetic injection, in treatment of asthma, (1941–2) 158
- Peritendinitis, crepitating, treatment by immobilization, (1939) 235
- Peritoneal
 - adhesions, heparin in, (1940) 452
 - cavity,
 - endoscopic examination of, (1944) 16
 - introduction of sulphanilamide into, (1941–2) 272
 - paraffinomas as result of liquid paraffin treatment, (1941–2) 330
 - immunity, (1944) 320
- Peritonoscopy, (1943) 103, (1944) 16

Peritoneum

- diseases, non-inflammatory, (1941–2) 329
- immunity and, (1944) 320
- parietal, sensitiveness of, (1940) 141
- sulphonamide compounds, effects of, (1943) 305
- tumours, (1941–2) 329
- Peritonism, diagnosis of, (1940) 443
- Peritonitis
 - acute, treatment by alcohol lavage, (1941–2) 330
 - adhesive, (1941–2) 330
 - appendicitis complicated by, (1939) 222, (1940) 190
 - children, in, treatment, (1940) 443
 - primary, (1940) 443
 - chronic, (1941–2) 330
 - diagnosis and differential diagnosis, (1940) 443
 - encapsulating, (1941–2) 271
 - immunity and, (1944) 320
 - pneumococcal, nephrosis complicated by, (1939) 444
 - prophylaxis, (1944) 14, 320
 - whole blood, by use of, (1940) 443
 - rupture of duodenum with fat necrosis and, (1943) 250
 - sulphonamides, local application of, in, (1941–2) 13
 - traumatic, diagnosis of, (1940) 443
 - treatment,
 - sulphanilamide, (1940) 190
 - surgical and chemotherapeutic, (1940) 443
- Permanent waving, hydrogen sulphide poisoning during, (1941–2) 410
- Pernicious anaemia, (1939) 203, (1940) 4, 6, 32, 168–170, (1944) 129
- achylia gastrica and, (1943) 47
- advances in knowledge of, (1940) 6
- aetiology, (1940) 168, (1941–2) 139
- hypopituitarism, (1944) 129
- angina pectoris complicating, (1940) 169
- argentaffin cells and, (1940) 168
- carcinoma of stomach complicating, (1944) 130
- Castle's intrinsic factor, (1943) 3, 47
- clinical picture, (1940) 168
- diagnosis, (1940) 169
- differential diagnosis, sprue, tropical, (1944) 378
- erythrocyte response to treatment, (1941–2) 139
- gastroscopy in, (1939) 203
- hepatic cirrhosis, association with, (1943) 268
- histological observations, (1944) 130
- hypopituitarism and, (1944) 129
- jaundice associated with, (1940) 168
- leukaemia associated with, (1939) 405
- nervous symptoms, vitamin B₁₂ therapy, (1940) 170
- pathology, (1944) 130
- phenols, volatile, excretion of, (1940) 169
- plasma-prothrombin in, (1941–2) 139
- prognosis, (1940) 169
- serum-bilirubin in, (1939) 203
- treatment, (1939) 203, (1941–2) 139
- liver extract, capacity to store, (1940) 170
- vitamin B₁₂, (1940) 170
- tuberculosis of stomach and, (1940) 169
- vitamin K plasma-prothrombin relation, (1941–2) 139
- Peroneal
 - muscular atrophy, (1939) 470
 - region, alopecia of, (1940) 165
- Personality *See also* Psychoses
 - changes in factory workers due to carbon disulphide intoxication, (1943) 365
 - development, (1944) 77
 - psychopathic, leucocytosis in, (1943) 315
 - rheumatoid arthritis, in, (1943) 136
 - types, and effort syndrome, (1941–2) 245
- Perthes's disease, (1940) 296
- Pertussis *See* Parapertussis, Whooping-cough
- Pervitin, (1944) 321
- Petechial haemorrhages, anti-syphilitic therapy causing, (1941–2) 405
- Pethidine hydrochloride, (1941–2) 113, (1944) 110
- clinical effects, (1944) 326
- pain, for relief of, (1944) 326
- Petrol, poisoning by, (1943) 363
- Petroleum jelly dressings, (1941–2) 264
- Petrositis, aetiology and surgery of, (1943) 199
- Petrous bone, fractures of, (1940) 49–53

CUMULATIVE INDEX

- Pfeiffer's bacillus
human infection with, (1943) 223
meningeal infection with, (1943) 279
- Phaeochromocytoma,
adrenal medulla, of, (1943) 107, 150
adrenals, of, (1944) 123
- Phagedaenic ulcer, (1941-2) 392
- Phakomas, tuberous sclerosis, in, (1943) 204
- Phantom limb, (1943) 76
- Pharmaceutical Codex, British* (Third and Fourth Supplements), (1943) 93
- Pharmacology, (1940) 444-63; (1941-2) 330, (1943) 93, 301, (1944) 320-9. *See also* under separate drug headings
- Pharmacopoeia, British*
additional monographs, (1941-2) 112
Fifth Addendum, (1942), (1943) 93
Fourth Addendum, (1941-2) 112
Second Addendum, (1940) 127
- Pharmacopoeia commission, (1944) 109
- Pharmacy and Medicines Act (1941), (1941-2) 111
- Pharyngo-pouch, surgical treatment, (1943) 309
- Pharyngitis
acute, and Vincent's angina, (1941-2) 349
chronic, Plummer-Vinson syndrome associated with, (1940) 463
streptococcal, sulphonamide therapy, (1940) 463
- Pharyngo-oesophageal sphincter, achalasia of, (1941-2) 128
- Pharynx
carcinoma of tonsil, (1941-2) 349
diseases, (1940) 463, (1941-2) 349
infections of, chemotherapy in, (1941-2) 60
larynx, and, treatment of malignant disease of, (1939) 90
polypoid fibro-lipomatosis pharyngis, (1941-2) 349
post-cricoid carcinoma, (1943) 309
pouch or diverticulum, (1943) 309
tumours, (1941-2) 349, (1943) 309
ulcers, decubital, (1941-2) 350
- Phenitone, (1940) 127
epilepsy treated with, (1940) 135
- Phenodol, (1944) 110
- Phenobarbitone
belladonna, and, epilepsy treated with, (1939) 332, (1941-2) 222
epilepsy treated with, (1940) 293
exfoliative dermatitis due to, (1941-2) 204
mentality of epileptics, effect on, (1940) 293
sodium (nembital), (1939) 163
- Phenolphthalein
constipation treated with, (1944) 190
liver, effect on, (1941-2) 288
test, gastro-intestinal disease, in, (1940) 544
ulceration of gastro-intestinal tract, in, (1941-2) 273
- Phenols, volatile, anaemia, pernicious, excretion in, (1940) 169
- Phenolsulphonphthalein (P S P) test, kidney function, of, (1940) 119
- Phenothiazine
anthelmintic, as, (1941-2) 122
ascariasis, in, (1941-2) 156
dermatitis caused by, (1940) 258
fatal poisoning with, (1944) 307
guinea-worm infestation treated by injections of, (1943) 228
oxyuriasis, in, (1943) 287
- Phenoxis, (1941-2) 122
- Phenytoin, soluble, (1941-2) 113, (1943) 95
- Phlebitis
aseptic, treatment of, (1943) 375
complications, prophylaxis and treatment of, (1943) 375
novocain infiltration of lumbar sympathetic, (1940) 582
- Phlebosclerosis, primary portal, in children, (1943) 351
- Phlebotomus argentipes*, kala-azar transmitted by, (1944) 97
- Phlebotomus* fever, (1940) 464
- Phlegmasia alba dolens, (1941-2) 296
- Phlyctenular ophthalmia, (1939) 129
- Pholedrine, (1944) 110
- Phonocardiography, (1939) 59
- Phosgene poisoning, (1940) 310
- Phosphatase
prostatic carcinoma, in, blood serum values, (1944) 337
serum, chronic arthritis in, (1940) 201
tumours of bone, production, in, (1941-2) 172
vitamin D deficiency, in, (1940) 116
- Phosphorus
chemical warfare, application in, (1944) 385
keratitis due to, (1944) 192
metabolism in thyrotoxicosis, (1941-2) 236, (1943) 223
poisoning, (1944) 385
lodging of exploding bullets, from, (1944) 19
radioactive,
cancer treated with, (1943) 171
leukaemia, effects in, (1943) 265
- Photofluoroscope, (1940) 104
- Phrenazol, (1941-2) 79 *See also* Cardiazol
leptazol, official name for, (1940) 127
- Phrenic nerve
injury, isolated unilateral, (1943) 290
paralysis, pulmonary tuberculosis, in, (1941-2) 292
- Phrenico-costal sinus pneumonia, (1941-2) 298
- Phrynodermia, (1939) 538
- Phthiocol, properties of, (1940) 590
- Phycomyces blakesleeanus*, use of, in estimation of vitamin B₁, (1940) 115
- Phylloquinone, (1940) 131 *See also* Vitamin K
- Physiological knowledge, necessity for, in surgery, (1939) 26
- Physiotherapy, (1941-2) 350
general practice, (1941-2) 350
refrigeration, (1941-2) 350
rheumatoid arthritis, (1941-2) 154
use in various medical conditions, (1944) 330
- Physolactin, (1939) 109, (1940) 132
- Physostigmine, action on plain muscle of, (1939) 164
- Phytic acid, national flour, in, (1944) 22
- Phytobezoar, surgical removal of, (1943) 353
- Pick's disease, (1939) 365, 506
pericardium, (1940) 332
- Picrotoxin, (1939) 164
barbiturate poisoning treated with, (1940) 558
convulsion therapy, use in, (1940) 59
- Pigmentary sarcoma, Kaposi's, (1943) 347
- Pigmentation, iron salts causing, (1940) 235
- Piles, rectal tumours after injection of, (1940) 506
- Pili torti, (1940) 328, (1941-2) 243
- Pilots *See* Aviation medicine, Aviators, flying
- Pine, aromatic oil of, (1943) 96
- Pineal body, tumours, (1939) 474, (1941-2) 350
hypogonadism associated with, (1939) 475
morbid anatomy, (1939) 474
- Pinelectomy, experimental, results of, (1941-2) 350
- Pingueculae, biopsy examination of, in Gaucher's disease, (1941-2) 287
- Pink disease, (1939) 475
general review, (1943) 310
nicotinic acid in treatment, (1943) 475
second attacks, incidence of, (1943) 310
treatment,
hepatex injections, (1944) 330
vitamin B₁, (1939) 475, (1940) 464, (1941-2) 50
- Pinna injuries, (1940) 46
- Pinworm *See* Oxyuriasis
- Pitressin (pituitary extract), (1939) 165
cardiovascular disease, effects in, (1941-2) 336
cholecystography, use in, (1940) 503
tannate, diabetes insipidus treated with, (1941-2) 205
- Pituitary extract
alcohol tolerance, effect on, (1939) 194
anterior lobe, (1941-2) 22
adrenal medulla, effect on, (1940) 152
anti-diabetogenic principle, (1941-2) 205
schizophrenia, in, (1940) 495
undeveloped uterus, in, (1939) 587
gonadotrophic, antagonism to pregnant mare's serum, (1941-2) 336
induction of labour, in, (1939) 395; (1941-2) 279

CUMULATIVE INDEX

Pituitary extract—*continued*

- posterior lobe, action on plain muscle, (1939) 164
 - diabetes insipidus treated by, (1941-2) 205
 - induction of labour, in, (1941-2) 279
 - non-gravid uterus, effect on, (1940) 453
- Pituitary fossa, X-ray examination of, (1944) 357
- Pituitary gland, (1944) 44
 - adenomas, (1940) 466
 - chromophobe, (1940) 466
 - extrasellar extension, (1940) 466
 - X-ray therapy, (1940) 467
 - advances in knowledge of, (1940) 4
 - alopecia, relation to, (1940) 165
 - anatomy and physiology, (1940) 465
 - anterior lobe,
 - diabetes mellitus and, (1944) 199
 - diabetogenic principle, (1943) 32, 185, 332
 - glycotropic principle, (1943) 32
 - hormones, (1941-2) 351, 382, (1943) 332
 - urine, in, (1944) 397
 - lactogen, (1943) 332
 - necrosis, acute, during puerperium, (1940) 465
 - oestrogens, effect of, (1940) 521, (1941-2) 382
 - oestrogens, synthetic, effect of, (1943) 333
 - growth, on, (1943) 302
 - pancreatrophic principle, (1940) 452, (1943) 32
 - post-partum necrosis, (1939) 36
 - Simmonds's syndrome, and, (1940) 530
 - specific metabolic stimulant in, (1939) 476
 - toxæmias of pregnancy, in, (1940) 480
 - urinary excretion, control of, (1939) 477
 - antihormones, (1944) 44
 - atrophy of, following tuberculosis, and Simmonds's syndrome, (1940) 531
 - diabetes insipidus and, (1940) 261, (1944) 46
 - diabetes mellitus and, (1940) 264
 - hypertension, and, treated by irradiation of, (1943) 152
 - diseases, (1939) 476, (1940) 465-7, (1941-2) 351
 - anterior lobe principles, (1939) 476
 - Cushing's syndrome, (1939) 478
 - endocrines in relation to, (1939) 14, 17
 - growth hormone, (1939) 476
 - hypopituitarism, (1939) 477
 - appendicectomy, after, (1939) 477
 - thyrotrophic hormone treatment, (1939) 477
 - Frohlich's syndrome, and, (1940) 152
 - functional activity, (1944) 44
 - genito-pituitary adiposity, in, (1940) 152
 - gigantism, hyperpituitary, (1940) 467
 - gonadotrophic activity, effect of oestradiol benzoate on, (1940) 521
 - growth, relation to, (1940) 281
 - headache due to hyperactivity of, (1940) 329
 - hormones,
 - anterior lobe, (1941-2) 351, 382, (1943) 332
 - growth hormone, (1941-2) 351
 - metabolism-stimulating, (1939) 189
 - ovarian follicle-stimulating, (1941-2) 382
 - purified interstitial cell-stimulating, (1941-2) 351
 - synergism of oestrogens with pituitary gonadotropins, (1941-2) 384
 - thyroidotrophic, (1941-2) 382
 - hypothalamic-pituitary syndromes, (1940) 465
 - hypothalamus, and, (1940) 66
 - Laurence-Moon-Biedl syndrome, (1941-2) 351
 - mongolism, in, (1939) 432, (1940) 408
 - myxoedema, in, (1943) 286
 - necrosis, acute, during puerperium, (1940) 465
 - pars nervosa, (1944) 87
 - physiology, (1941-2) 351
 - plain muscle, action of posterior lobe on, (1939) 164
 - posterior lobe,
 - fractured skull and injury to, (1941-2) 174
 - gastric changes following injury, (1941-2) 174
 - hypertension, relation to, (1940) 211
 - peptic ulcer, insufflation of powder in, (1940) 441
 - plain muscle, action on, (1939) 164
 - post-partum uterus, effect on, (1940) 498
 - preparations, in obstetrics, (1941-2) 16
 - schizophrenia, in, (1940) 495
 - stalk, division of, (1940) 262
 - synergist, (1941-2) 22

Pituitary gland—*continued*

- tumours, (1939) 478, (1940) 466
 - hypophysectomy, complete, for, (1943) 310
 - X-ray therapy, (1940) 467
- undescended testes, in relation to, (1939) 561
- water balance and, (1940) 261
- Pituitrin, in blood of pregnant women, (1941-2) 278
- Pityriasis rosea, convalescent serum in treatment, (1940) 467
- Placenta, (1944) 330
 - ischaemia of, and eclampsia, (1944) 24
 - luteinizing principle from, (1941-2) 22
 - sulphanilamide, transmission of, (1940) 458
 - visualization by soft-tissue radiography, (1941-2) 280
 - vitamin C content, (1940) 141
- Placental
 - blood, transfusion of, (1940) 38, 221
 - circulation, (1943) 15
 - extract, prophylaxis of measles, in, (1941-2) 302
- Plague
 - epidemiology, (1943) 85
 - M & B 693 in treatment of, (1939) 479
 - sulphathiazole in prophylaxis and treatment, (1940) 468
 - sulphonamides in, (1943) 85
 - vaccines in prophylaxis, (1939) 148
- Plantigrathy, (1940) 101
- Plantar warts, X-ray and radium therapy for, (1941-1942) 393
- Plants, dermatitis caused by, (1941-2) 202
- Plasma *See also* Blood, plasma
 - lipids, obstructive jaundice and hepatic disease, in, (1943) 148
 - prothrombin, normal level, effect of vitamin K on, (1943) 378
- Plasmacytoma of lacrimal gland, (1939) 397
- Plasma-fibrinogen, in repair of peripheral nerve lesions, (1941-2) 94
- Plasma-prothrombin
 - pernicious anaemia, in, (1941-2) 139
 - titrations in infants, (1941-2) 241
- Plasmodium
 - falciparum, malaria, in, (1940) 76
 - ovale, malaria, in, (1943) 276
- Plasmoquine, (1941-2) 112
 - malaria, in treatment of, (1939) 144, (1940) 76, (1943) 82
- pamaquin, official name for, (1940) 127
- Plaster of Paris
 - closed method, (1940) 350
 - bacteriology of wounds treated by, (1941-2) 267
 - burns treated by, (1943) 169
 - war surgery, use of, in, (1940) 9
 - windowed unpadded casts, (1941-2) 265
- Plastic
 - surgery, (1941-2) 12
 - sutures, synthetic, (1941-2) 264
- Platelets, blood *See* Blood platelets
- Plethysmographic method of measuring peripheral blood flow, (1941-2) 151
- Pleura
 - cyst of, (1940) 394
 - diseases, (1941-2) 71, (1943) 58
 - drainage in war wounds, (1943) 249
- Pleural
 - effusion,
 - radiography in (1941-2) 352
 - simultaneous bilateral, (1940) 468
 - treatment, (1944) 293
 - tuberculous, eosinophilia in, (1941-2) 291
 - pain, procaine in, (1940) 473
- Pleurisy, (1941-2) 352
 - amoebic hepatic abscess, complicating, (1940) 167
- Pleurotomy, in treatment of complications of artificial pneumothorax, (1940) 391
- Plummer-Vinson syndrome, (1939) 43, (1940) 146, (1943) 104
 - pharyngitis, chronic, and, (1940) 463
 - radiological observations, (1941-2) 128
- Pneumococcal meningitis *See also* Meningitis, pneumococcal
 - chemotherapy in, (1943) 280

CUMULATIVE INDEX

Pneumococcus
 endocarditis, malignant, caused by, (1944) 249
 infection,
 sulphapyridine in, (1941-2) 342
 sulphonamides in, (1941-2) 342
 M & B 693, effect of, on, (1939) 171
 metabolism, effect of sulphonamides on, (1941-2) 342
 polysaccharide, in prophylaxis of pneumonia, (1941-2) 355
 sulphamylamide, action on, (1940) 133
 sulphapyridine, effect on, (1940) 133
 sulphonamides, action on, (1939) 171
 types, in lobar pneumonia, (1944) 331
Pneumolysis
 extra-pleural, tuberculosis, pulmonary, in, (1940) 95
 internal, tuberculosis, pulmonary, in (1940) 393
Pneumectomy, (1943) 272
 carcinoma of bronchus, for, (1943) 60
 respiration, effects upon, (1944) 295
 total, (1944) 294
 bronchial carcinoma, for, (1944) 69
Pneumonia, (1941-2) 3
 aspiration, (1941-2) 177, (1943) 166
 atypical, (1944) 169
 aetiology, (1944) 169
 classification, (1944) 169
 clinical picture, (1944) 169
 infective agent, (1944) 41
 virus strains, (1944) 170
 identification of, (1944) 41
 X-ray findings, (1944) 169
 biliary colic complicated by, (1943) 219
 chicken-pox complicated by, (1943) 173
 clinical picture and treatment, (1941-2) 177
 lipid, (1943) 166, 310
 iodized oil, due to, (1944) 331
 nasal sprays cause of, (1939) 285
 lobar, (1939) 479, (1941-2) 352, (1943) 310, (1944) 331
 artificial pneumothorax, (1939) 483
 bacteriology, (1939) 13, 479, (1944) 331
 children, in, (1941-2) 355
 complications and sequelae, (1944) 332
 course and prognosis, (1941-2) 352
 eosinophilia, prognostic significance of, (1940) 468
 experimental infection in dogs, (1944) 331
 gastric and renal complications, (1939) 480
 hydroxyethylapocuprene, (1939) 483
 infants, in, (1941-2) 352
 jaundice associated with, (1944) 332
 lipid, due to iodized oil, (1944) 331
 mortality and sulphonamide compounds, (1941-1942) 352
 oxygen administration, (1939) 483
 passive immunity against, (1939) 16
 pathogenesis, (1944) 331
 pleural pain, procaine injection for relief of, (1940) 473
 pneumococcal, (1941-2) 352
 pneumococci, types of, (1944) 331
 prognosis, (1940) 468
 prophylactic effect of pneumococcus polysaccharide in old age, (1941-2) 355
 serum therapy, (1939) 482
 sputum, (1941-2) 352
 sulphonamide drugs, (1939) 17, 480
 with serum, (1939) 481
 treatment, (1940) 469-74, (1941-2) 352
 combined chemotherapy and serum therapy, (1941-2) 354
 cortin and sodium chloride, (1941-2) 355
 hydroxyethylapocuprene and sulphapyridine, (1941-2) 354
 oxygen, (1940) 473
 sodium sulphapyridine intravenously, (1940) 471, (1941-2) 354
 soluble sulphapyridine, (1940) 471
 sulphadiazine, (1944) 332
 sulphanilamide and amidopyrine, (1940) 234

Pneumonia—continued
 lobar—continued
 treatment—continued
 sulphapyridine, (1940) 469-73, (1941-2) 353
 barbiturates, and, (1940) 472
 hydroxyethylapocuprene dihydrochloride, and, (1940) 472
 serum, and, (1940) 472
 sulphathiazole, (1941-2) 352-4
 sulphapyridine, and, (1940) 473
 sulphonamide drugs, (1940) 469-73, (1941-2) 352
 X-ray, (1940) 474, (1941-2) 355
 phrenico-costal sinus, (1941-2) 298
 pneumococcal, (1943) 311
 positive syphilitic reactions in, (1943) 89
 treatment,
 chemotherapy, (1943) 306
 serum, and, (1943) 310
 radiotherapy, (1939) 514
 sulphapyrazine, (1943) 311
 sulphathiazole, (1941-2) 177
 sulphonamide compounds, (1941-2) 177
 young adults, in, (1941-2) 177
Pneumonitis
 aspiration, (1940) 235
 primary virus, (1943) 273
Pneumoperitoneum, pulmonary tuberculosis treated by, (1943) 269
Pneumopneumothorax, in diagnosis of calculi, (1940) 368
Pneumothorax
 artificial,
 abdominal conditions, acute, differential diagnosis, (1940) 391
 accidents and complications, (1940) 390
 air embolism complicating, (1943) 128
 ambulatory, (1944) 292
 cavities, tuberculous, significance of, (1944) 70
 chest wounds, in, (1940) 349
 complications, treatment of, (1940) 391
 end-results, (1940) 392
 pleural effusions complicating, (1944) 293
 pleurotomy in, complications, (1940) 391
 psychotic patients, in, (1940) 391
 pulmonary tuberculosis, in, (1944) 70
 results and complications, (1941-2) 293
 sputum, rate of conversion of, (1940) 391
 embolism causing, (1941-2) 290
 pulmonary infarction causing, (1941-2) 290
 spontaneous, (1939) 484, (1940) 474
 constant suction, apparatus for, in, (1940) 475
 haemopneumothorax, treatment of, (1943) 311
 systolic 'clicks' in, (1940) 474
 tense or valvular, iodized poppy-seed oil in treatment of, (1939) 484
 treatment, (1940) 475, (1943) 311
 valvular type, (1940) 475
Poisoning, (1940) 554-63, (1941-2) 408, (1944) 384-9
 abortifacients, (1940) 559
 accidental, (1943) 363
 alkaloids, (1940) 556
 ammonia, (1943) 363
 barbiturates, (1940) 557
 cadmium, (1943) 6, 364
 cyclic ureides and barbituric acid, (1940) 557
 gases, (1940) 554
 homicidal, suicidal and accidental, (1941-2) 408
 industrial, (1940) 559-63, (1941-2) 411, (1943) 364
 benzene, (1940) 560-2, (1944) 387
 carbon disulphide, (1943) 365
 chlorinated naphthalene, (1944) 387
 fluorides, (1944) 386
 fluorine and compounds, (1940) 560
 gases, irritant, (1944) 386
 lead, (1944) 387
 magnesium, (1944) 386
 manganese, (1940) 560
 mercury fulminate, (1940) 559
 new dangers, (1944) 388
 nitro- and amino-derivatives, (1940) 562
 oral hygiene, importance of, (1944) 386
 phosphorus, (1944) 385
 radium, (1940) 563
 solvents, volatile, (1944) 387
 teeth, effect on, (1944) 386

CUMULATIVE INDEX

- Poisoning—continued**
industrial—continued
 toluene, (1943) 364
 trinitrotoluene, (1943) 365
 tri-*ortho*-cresyl phosphate, (1944) 389
 vanadium, (1940) 562
 mercury, (1943) 364
 metallic, (1940) 555
 organic substances, synthetic, (1940) 554
 paraldehyde, (1943) 363
 petrol, (1943) 363
 Poison ivy dermatitis, (1941-2) 203
 Poisons, (1941-2) 408
 Polioencephalitis
 haemorrhagica superior, (1940) 69
 Wernicke's vitamin B deficiency associated with, (1941-2) 369
 Poliomyelitis, (1940) 476, (1941-2) 356, (1944) 332
 aetiology, (1940) 476, (1941-2) 356, (1944) 38, 332
 antibodies, formation of, (1941-2) 356
 bacteriology, (1940) 476
 bulbar, after tonsillectomy, (1943) 362
 diagnosis, (1940) 476
 epidemiology, (1941-2) 356, (1944) 38
 experimental, in animals, (1940) 476
 field of contagion in children, (1941-2) 356
 immunity and immunization, (1944) 39
 resistance, (1941-2) 356
 infected drain water, (1940) 476
 'interference' phenomenon, (1944) 40
 intradermal test for, (1940) 476
 mode of virus invasion, (1944) 88
 neural mechanisms in, (1944) 88
 olfactory mucosa in, (1941-2) 356
 paralytic stage, (1944) 333
 polioencephalitis, and, (1939) 484
 aetiology, (1939) 484
 children, in, (1939) 42
 clinical picture, (1939) 485
 diagnosis, (1939) 485
 exercises, under-water, in treatment, (1939) 486
 Pettit's serum, (1939) 486
 zinc sulphate in prophylaxis, (1939) 485
 process of invasion, (1944) 39
 stools, toxic factor in, (1941-2) 356
 tonsillectomy and, (1941-2) 356, (1944) 39
 infection after, (1944) 332
 treatment,
 Kenny, (1944) 333
 potassium chlorate, (1940) 477, (1941-2) 357
 protosol soluble, (1940) 476
 serum injections, (1941-2) 357
 sulphapyridine and anti-serum, (1941-2) 356
 sulphonamides, (1941-2) 49
 virus, (1944) 38
 mode of invasion, (1944) 88
Pollen
 antigen hydrochloride, use of, (1944) 128
 contact, and age of onset in hay fever, (1941-2) 137
 desensitization, (1943) 112
 extract,
 oil, in, hay fever treated with, (1944) 128
 skin sensitivity, and, (1941-2) 137
 slow-absorbing, in hay fever, (1941-2) 136
 oral, in treatment of hay fever, (1941-2) 137
 Polya gastrectomy, (1940) 13
Polyadenomes
en nappe, (1943) 352
polypyeux, (1943) 352
 Polyarteritis nodosa, (1943) 348
 Polyarthritis, hydrotherapy in, (1939) 377
 Polycystic disease of kidney, (1941-2) 275
 Polycythaemia
 experimental, (1941-2) 225
 vera, radiological diagnosis, (1943) 206
 Polymyositis, (1944) 306
 Polyneuritis. *See also* Neuritis, multiple
 acute infective, (1943) 291
 aneurin in alcoholic, (1939) 18
 toxic, sulphamethylthiazole causing, (1943) 291
 Polyostotic fibrous dysplasia, (1944) 162
- Polypi**
 colon, of, (1940) 250, (1944) 184
 multiple primary, (1941-2) 195
 gastric, (1944) 380
 intestinal, (1941-2) 375
 oesophagus, of, (1944) 313
 rectal, (1940) 506
Polypoid
 fibro-lipomatosis pharyngis, (1941-2) 349
 gastritis, (1944) 380
Polyposis
 gastric, (1943) 352
 intestine, of, (1941-2) 375
 differential diagnosis, (1941-2) 375
 precursor of carcinoma, (1941-2) 375
 small intestine, of, (1939) 388
 Polyradiculitis, mumps complicated by, (1941-2) 309
 Polysaccharides, antigenic capsular, in prophylaxis of pneumonia, (1941-2) 355
 Polyuria, diabetes insipidus, in, (1940) 66
 Pons, tumours of, (1940) 230
 Poor, aged, care of, (1941-2) 379
 Popliteal space, sarcoma of, (1940) 570
Porphyria
 acute, (1943) 228
 porphyrinuria, without, (1940) 323
 chemistry of, (1940) 323
 excretion after antipyretics, (1940) 324
 metabolism, (1940) 119
Porphyrim excretion
 anaemias, in, (1943) 25
 methyl chloride poisoning, in, (1941-2) 411
Porphyria
 antipyretics causing, (1940) 324
 chemical workers, in, (1940) 562
 epidermolysis bullosa, in, (1940) 533
 nicotinic acid in, (1940) 129
 porphyria, acute, without, (1940) 323
 psychotic symptoms with, (1940) 324
 sulphonamides causing, (1940) 324
 tests for, (1943) 25, 365
 trinitrotoluene poisoning, in, (1943) 365
Portal
 phleboscлерosis, primary, in children, (1943) 351
 vein, phlephlebitis, suppurative, (1941-2) 288
 Portmann's operation, labyrinthine vertigo, for, (1940) 583
 Port-wine stain, Grenz ray therapy, (1940) 187
 Post-cricoid carcinoma, (1943) 309
 Posterior fornix, needle puncture of, (1940) 23
 Post-mortem examination, (1939) 487
 bloodstains, (1939) 487
 sub-clinical lesions, (1939) 487
 Post-partum necrosis of anterior pituitary, Simmonds's syndrome and, (1940) 530
Posture
 electrocardiogram, effect on, (1944) 247
 hypotension and, (1940) 217, (1941-2) 166
 treatment of shock, in, (1941-2) 387
 Post-vaccinal meningo-encephalo-myelitis, (1943) 201
Potassium
 Addison's disease, in, (1940) 154
 blood, in, (1940) 219
 chlorate,
 black hairy tongue treated with, (1940) 411
 poisoning, (1940) 556
 poliomyelitis, use in, (1940) 477, (1941-2) 357
 chloride,
 allergic conditions, in, (1940) 161, 164, (1941-2) 136
 extrasystoles, in, (1941-2) 150
 familial periodic paralysis, in, (1939) 166
 periodic paralysis, in, (1940) 68
 erythrocytes, diffusion from, (1940) 219
 iodide, relative value as expectorants of ipecacuanha and, (1940) 453
 test, leprosy, in, (1940) 381
 metabolism, (1940) 113
 allergic conditions, in, (1940) 113
 paralysis, familial periodic, in, (1940) 114
 shock, in, (1940) 113
 muscular diseases, in, (1940) 68
 myasthenia gravis, role in, (1940) 416

CUMULATIVE INDEX

Potassium—*continued*

- nitrate, Mènière's syndrome treated with ammonium chloride and, (1940) 584
- periodic paralysis in relation to, (1940) 68
- permanganate, as antiseptic, (1944) 13
- plasma concentration and toxicity, (1940) 219
- plasma, in shock, (1940) 528
- salts,
 - allergic conditions, in, (1940) 161, 164
 - anuria, and, (1941-2) 408
 - hay fever treated with, (1940) 161
 - vasomotor rhinitis treated with, (1940) 162
- tellurite test, diphtheria, in, (1940) 272
- thiocyanate, hypertension, in, (1940) 213
- poisoning by, (1944) 384
- tolerance curve, diagnosis of Addison's disease, in, (1941-2) 131
- Pott's disease, (1941-2) 396 *See also* Spine, tuberculosis
- Praequine, pamaquin, official name for, (1940) 127
- Prausnitz-Kustner reaction, (1940) 278
- Precancerosis, (1941-2) 394
- leucoplakia and keratoses, (1941-2) 394
- Precocity, interstitial-celled tumour of testis and, (1941-2) 405
- Pte-clempsia
 - hypertension and, (1941-2) 18
 - renal damage, permanent, after, (1940) 17
- Prefrontal
 - leucotomy, in treatment of mental disease, (1943) 67, 316
 - lobotomy, treatment of mental disease by, (1941-2) 365
- Preganglionic denervation, (1944) 81
- Pregnancy, (1944) 333 5
 - adrenal haemorrhage in, (1941-2) 358
 - alopecia totalis during, (1940) 165
 - anaemia, (1944) 22
 - haemolytic (I ederer), (1944) 132
 - hypochromic, (1940) 171
 - iron and diet, effect of, (1940) 187
 - macrocytic hyperchromic, (1944) 131
 - megalocytic, (1940) 171, (1944) 130
 - war-time, in, (1944) 133
 - antuitrin-S skin test, (1939) 489
 - blood in, oxytocic substance and pituitrin, (1941-2) 278
 - calcium requirements, (1944) 22
 - cardiovascular system, diseases of, (1939) 491
 - heart disease, (1939) 491
 - varicose veins, (1939) 492
 - cervical, (1940) 481
 - Clostridium welchii*, infection in, (1940) 481
 - cold-pressor test, (1940) 479
 - combined, (1940) 479
 - diabetes mellitus in, (1939) 308, (1941-2) 16, (1944) 201
 - diagnosis, (1940) 478, (1941-2) 357
 - antuitrin-S skin test, (1941-2) 357
 - Aschheim-Zondek test, (1939) 488
 - modification of, (1940) 478
 - Friedman test, (1940) 478, 481, (1941-2) 358
 - simplified tests for, (1944) 23
 - urinary excretion of pregnanediol, (1941-2) 357
 - xenopus test, (1941-2) 358
 - diet in, (1944) 142-5
 - diphtheritic antitoxin level in, (1941-2) 260
 - ectopic, (1943) 207
 - needle puncture of posterior fornix in, (1940) 23
 - pre-existing tubal infection, and, (1941-2) 228
 - endometrium, changes in, (1940) 477
 - erythema palmaris hereditarium and telangiectases associated with, (1943) 205
 - extra-uterine and intra-uterine, simultaneous, (1940) 479
 - foetal heart, electrocardiographic record of, (1939) 489
 - Friedman test, (1940) 478
 - haemorrhages of, (1941-2) 358
 - heart disease in, (1944) 335
 - Hodgkin's disease in, (1944) 252
 - hormones in, (1940) 478, (1941-2) 357
 - hyperemesis gravidarum, (1939) 489, (1940) 479, (1941-2) 358

Pregnancy—*continued*

- hypertension, essential, in, (1939) 491, (1944) 334
 - hypoparathyroidism in, (1941-2) 323
 - hypovitaminosis B₁ and E in, (1944) 142
 - infections, (1940) 481
 - leucorrhoea in, (1940) 19
 - mineral requirements, (1944) 143
 - myotic infections of vagina during, (1940) 594
 - non-convulsive toxæmia in, (1940) 17
 - normal and pathological, (1939) 488
 - nutrition in, (1944) 22, 142-5
 - ovarian, Friedman test in, (1940) 481
 - oxytocic substance and pituitrin in blood, (1941-2) 278
 - pelvic osteoarthropathy of, (1940) 482
 - physiology, (1940) 477, (1941-2) 357
 - polynecrosis, (1939) 492
 - posterior pituitary preparations in, (1941-2) 16
 - pre-eclamptic toxæmia and eclampsia, (1939) 490
 - cold-pressor test, (1939) 490
 - short-wave therapy, (1939) 491
 - pregnanediol excretion, (1941-2) 18, 357
 - pregniotin test, (1940) 478
 - protein requirements, (1944) 143
 - pyelitis of, (1940) 480, 501, (1941-2) 19
 - renal aneurysm, rupture of, (1944) 25
 - rheumatic heart disease in, (1944) 335
 - serological tests in, (1944) 25
 - soft-tissue radiography in, (1941-2) 280
 - splenic aneurysm, rupture of, (1944) 25
 - stilboestrol, effects of, (1941-2) 383
 - syphilis in, (1944) 24
 - thyroid gland in, (1940) 478
 - toxæmias of, (1940) 480, (1941-2) 358, (1944) 334 *See also* Eclampsia
 - aetiology, (1940) 479
 - anterior pituitary-like hormone in, (1940) 480
 - avitaminosis B₁ and, (1940) 479
 - classification of, (1941-2) 18
 - diet, (1944) 22
 - hydration, and, in treatment, (1940) 480
 - hormone factors in, (1940) 18
 - hypertension, essential, and, (1943) 16, 312
 - nephrosclerosis and, (1941-2) 357
 - pre-eclamptic and eclampsia and renal, (1941-2) 18
 - pyelitis, relation to, (1940) 480
 - renal damage, permanent, after, (1940) 17
 - retinal spasm in, (1940) 18
 - treatment, (1940) 480
 - tubal *See also* Tubal pregnancy
 - early recognition of, (1943) 207
 - needle puncture of posterior fornix in, (1940) 23
 - tuberculin testing, during, (1940) 481
 - tuberculosis in, (1940) 95, 481
 - tumours complicating, adenocarcinoma of kidney, (1944) 278
 - ureter, hormonal influences on, (1944) 23
 - vitamin
 - deficiency in, (1944) 142
 - requirements in, (1944) 143
 - vomiting of, (1941-2) 358
 - vulvo-vaginitis, (1939) 492
 - X-ray examination in, (1941-2) 280
- ## Pregnanediol
- excretion of, (1940) 21
 - pregnancy, during, (1941-2) 18
 - removal of ovarian tissue, after, (1941-2) 357
 - pregnancy toxæmias, in, (1940) 18
 - urinary excretion in pregnancy, (1941-2) 357
- ## Pregnennolone, (1943) 95
- abortion, treatment of, in, (1941-2) 126
- ## Pregnennol
- amenorrhoea, in, (1939) 202
 - meno-metrorrhagia in, (1940) 407
- ## Pregniotin test, pregnancy, for, (1940) 478
- ## Premature infant, caloric intake, (1943) 246
- ## Prematurity, (1939) 493
- dietetic deficiency causing, (1944) 22
 - oestrin in treatment, (1940) 482
 - vitamin B₁ in diet, (1939) 493
 - vitamin C in diet, (1939) 493
- ## Pre-menstrual salivary syndrome, (1940) 434
- ## Pre-senile and senile psychoses, (1941-2) 84

CUMULATIVE INDEX

- Pressor substances, (1941-2) 165
 blood, in, (1940) 5
 clampsia, and, (1941-2) 18
 Pressure, intermittent positive, in treatment of crush syndrome, (1944) 272
 Presystolic murmur, Austin Flint's, (1943) 239
 Pretibial myxoedema, in thyrotoxicosis, (1944) 307
 Preventive medicine, (1939) 4, 7
 Prickly heat, clinical types of eruption, (1944) 335
 Primigravidae, elderly, complications in, (1944) 298
 Primogeniture, congenital pyloric stenosis, in, (1940) 501
 Printers
 benzene poisoning in, (1941-2) 411
 lead poisoning in, (1941-2) 282
 Procaine
 adrenaline, and, (1941-2) 112
 detoxification products in urine, (1944) 327
 fibrositis treated by injections of, (1943) 209
 herpes zoster, in, (1939) 374
 hydrochloride,
 injection into scalenus anticus muscle, (1941-2) 189
 injections for ischialgia, (1939) 239
 local anaesthetic, as, (1941-2) 142
 thrombophlebitis, in, (1940) 583
 injections for sprains, (1941-2) 159
 pleural pain, in, (1940) 473
 sciatica treated with, (1944) 364
 spinal anaesthesia, in, (1939) 209
 subarachnoid injection of, (1944) 327
 Proctocaine, ocular pain treated by retrobulbar injection of, (1941-2) 244
 Proctoscopy, diverticulitis, in, (1944) 207
 Profession, as factor in longevity, (1941-2) 379
 Proflavine
 antiseptic, as, (1944) 13
 snuff, (1941-2) 331
 bacteriostatic value, (1941-2) 330
 nasal sepsis and post-operative scarlet fever, prevention of, (1941-2) 330
 powder, (1944) 13
 sulphate, (1943) 95
 Progesterol, (1943) 95
 Progesterone, (1943) 95, 334
 absorption of subcutaneously implanted tablets, (1940) 453
 Addison's disease, effect on, (1940) 155
 amenorrhoea treated with, (1943) 114
 antitumorigenic action, (1940) 527
 carcinoma of breast treated with, (1943) 164
 diabetes mellitus during menopause treated with, (1941-2) 191
 endometrial hyperplasia, in, (1940) 288
 habitual abortion, in treatment of, (1939) 30
 implantation of, (1941-2) 384
 menorrhagia, in, (1939) 430
 menstrual and climacteric disorders treated with, (1941-2) 384
 milk secretion, action on, (1939) 220, 264
 ozaena, in, (1939) 453
 stilboestrol, adjunct to, (1940) 132
 Progestogens, (1944) 49
 Prognon
 blood pressure, effects on, (1941-2) 382
 peptic ulcer, in, (1940) 441
 Prognon B, cervix, effect on, (1940) 22
 Prokayvit, (1940) 131 *See also* Vitamin K
 Prolactin
 breast milk increased by, (1939) 35
 nursing women, effect in, (1940) 346
 therapeutic use of, (1940) 132
 Prolan
 habitual abortion, in treatment of, (1939) 30
 human ovary, effect on, (1941-2) 22
 large dosage, effect of, (1941-2) 22
 pituitary syneigist and, (1941-2) 22
 pregnancy,
 diagnostic test for, (1944) 23
 toxaemias, in, (1940) 18
 Proluton, (1943) 95
 cervix, effect on, (1940) 22
 Promanide, (1944) 114
 Promin, (1941-2) 119, (1944) 114
 blood levels, (1941-2) 337
 experimental tuberculosis, effect on, (1941-2) 336
 pulmonary tuberculosis, in, (1943) 62
 streptococcal infection, in, (1941-2) 336
 tuberculosis treated with, (1944) 393
 Prominal
 epilepsy treated with, (1940) 294
 phenitoin, official name for, (1940) 127
 Prontosil
 abortus fever, in, (1939) 183
 cerebrospinal fever, in, (1940) 244
 chancroid, in, (1939) 278
 chemistry and pharmacology of, (1939) 169
 convulsions in infancy, in, (1939) 291
 M & B 693, and, enteric fevers, in, (1939) 330
 malaria, in, (1939) 424
 red, undulant fever, in, (1939) 584
 soluble,
 colitis, ulcerative, in, (1940) 249
 local application of, (1940) 461
 poliomyelitis, in, (1940) 476
 therapy, trachoma, (1941-2) 412
 Prontosil S *See* Azolsulphamide
 Propadine hydrochloride
 allergic conditions treated with, (1940) 164
 intravenous drip administration, (1941-2) 346
 Propamide, (1944) 126
 burns, treated with, (1944) 322
 infected, treated with, (1944) 173
 wounds, treated with, (1944) 322
 infected, treated with, (1944) 269
 Proprietary drugs
 names of, (1941-2) 113
 official names for, (1940) 127
 Propyl hydroxybenzoate, (1943) 96
 Proseptasine, (1940) 133
 chemistry and pharmacology of, (1939) 170
 material prophylaxis, in, (1939) 423
 Prostate
 adenomatous enlargement, unilateral, (1943) 313
 calculus, (1940) 482
 trans-urethral removal, (1941-2) 361
 carcinoma, (1939) 495
 acid phosphatase, values of blood serum in, (1944) 337
 diagnosis early, importance of, (1944) 336
 direct extension to ureter in, (1941-2) 361
 testicular androgens, role of, (1944) 336
 testosterone propionate, effect of, (1940) 484
 treatment
 castration, (1943) 313, (1944) 94
 stilboestrol, (1944) 93
 diseases, (1939) 493 (1940) 482-5, (1941-2) 359, (1944) 92, 335 7
 massage effects of, (1939) 495
 enlargement,
 endoscopic methods in surgery of, (1940) 14
 hormone therapy in, (1940) 14, (1944) 50
 largest recorded prostate, (1941-2) 360
 pyelography intravenous, in, (1941-2) 360
 simple, (1939) 493, (1941-2) 360
 diagnosis and differential diagnosis, (1941-2) 360
 general review of, (1943) 313
 hemi-prostatectomy for, (1943) 313
 incidence, (1941-2) 360
 post-prostatectomy obstruction, (1944) 336
 renal dysfunction in, (1943) 313
 hormones in, (1939) 158, 535
 perineal prostatectomy for, (1944) 336
 sodium bicarbonate, intravenous, (1939) 494
 surgery, (1939) 494
 testosterone propionate, (1939) 494
 transurethral resection for, (1944) 335
 urine, measurement of residual, (1939) 494
 surgical treatment, indications, (1944) 92
 testosterone propionate in, (1940) 132, 483
 treatment, (1944) 92
 hormone therapy, in (1944) 93
 perurethral resection, (1944) 92
 resection, technique of, (1944) 92
 testosterone propionate, (1941-2) 360
 X-ray examination, (1941-2) 360
 lymphosarcoma of, (1943) 313

CUMULATIVE INDEX

Prostate—*continued*

- malignant disease, (1940) 484, (1941-2) 361
- diagnosis, early, importance of, (1944) 336
- obstruction, transurethral resection and prostatectomy, comparison of, (1940) 483
- recent work on, (1944) 92
- rhabdomyosarcoma, (1939) 495, (1940) 484
- testosterone propionate, histopathological effect of, (1940) 484
- transurethral resection and prostatectomy, comparison of results, (1940) 483
- tuberculosis of, (1941-2) 359
- Prostatectomy
 - obstruction following, (1944) 336
 - perineal, (1944) 336
- Prostatitis, treatment with staphylococcus toxoid, (1941-2) 359
- Prostigmin
 - Addison's disease, in, (1939) 166
 - calculus, ureteral, in, (1940) 369
 - chronic, (1941-2) 201
 - deafness, in, (1939) 296, (1943) 182
 - glaucoma, in, (1939) 350
 - intra-arterial injection of, (1943) 303
 - megacolon, in, (1939) 426
 - menstruation, delayed, in, (1940) 166
 - methylsulphate,
 - deafness and tinnitus aurium treated with, (1941-2) 201
 - morphine in relief of pain, with, (1941-2) 338
 - myasthenia gravis, in, (1939) 419, (1940) 417, (1943) 284
 - myotonia atrophica, in, (1940) 68
 - peripheral circulatory disturbances, in, (1940) 196
 - peristalsis stimulated by, (1939) 165
- Prostitutes, syphilis in, (1944) 382
- Protamine hexamine insulin, (1940) 267
- Protamine insulin, (1940) 265
 - diabetes mellitus, in, (1939) 67, 69
 - chemical composition and physiological action, (1939) 67
 - mixed injections, (1939) 70
 - therapeutic use, (1939) 68
 - zinc protamine insulin, (1939) 68, 70
- Protamine zinc insulin, clear, (1943) 34
- Protein
 - anaemia, in treatment of, (1939) 54
 - serum, (1941-2) 305
 - wound healing, in, (1941-2) 268
 - wounds, in, (1941-2) 263
- Prothrombin
 - blood levels, effect of vitamin K on, (1940) 590
 - deficiency,
 - haemoptysis and pulmonary tuberculosis, in, (1943) 230
 - haemorrhagic conditions due to, (1943) 24
 - new-born, in, (1940) 16, 31
 - post-operative, in obstructive jaundice, (1941-42) 273
 - dicoumarin, effect of, (1944) 322
 - level, effect of vitamin K, (1941-2) 427
 - plasma, in, (1940) 117
 - level, effect of vitamin K on, (1943) 378
 - pernicious anaemia, in, (1941-2) 139
 - response to vitamin K, as liver function test, (1944) 288
 - Russell's viper venom technique, estimation by, (1941-2) 163
 - test, (1940) 386
 - time in new-born, effect of vitamin A, (1941-2) 427
 - vitamin K and, (1940) 117, 131
- Protozoal disease
 - chemotherapy in, (1940) 78
 - diamidines in, (1941-2) 100
- Proxzekia trachomatis*, (1940) 564
- Prurigo
 - annularis, (1941-2) 361
 - hebra, (1941-2) 361
- Pruritus
 - ani,
 - faecal soiling of perianal skin and, (1941-2) 147
 - mercuric sulphide tattooing, (1939) 496, (1940) 189
 - general and blood cholesterol, (1944) 337
 - senile, oestrogen therapy, (1944) 337

Pruritis—*continued*

- vulvae,
 - magnesium sulphate injections in, (1940) 593
 - stilboestrol cream, use of, (1941-2) 430
 - stilboestrol therapy, (1940) 132
- Pseudo
 - acromegaly, (1943) 105
 - appendicitis, rheumatic, (1941-2) 378
 - Aigyll Robertson pupil, (1944) 149
 - fractures of bone, (1941-2) 171
 - haemophilia, gastric haemorrhage in, (1943) 229
 - hermaphroditism,
 - adrenal cortex, hyperplasia of, and, (1940) 155
 - dysgerminoma in, (1943) 294
 - laryngocoele, (1941-2) 311
 - paralysis, Parrot's, (1941-2) 404
 - sexual precocity, (1939) 192
 - thrombotic occlusion, femoral artery, of, (1940) 195
- Pseudomonas pyocyanea*
 - infection and chronic arthritis, (1944) 152
 - wounds infected by, (1941-2) 267
- Pittacosis, (1939) 496
 - clinical picture, (1940) 484
 - complement-fixation test, (1940) 485
 - sulphapyridine, treatment with, (1941-2) 361
- Psoriasis, (1939) 496, (1941-2) 362, (1944) 338-40
 - aetiology, (1941-2) 362
 - cholesterolaemia in, (1944) 338
 - low fat diet in, (1939) 496
 - metabolic disturbances in, (1941-2) 362
 - modern views on, (1944) 339
 - nails, X-ray therapy for, (1941-2) 362
 - syphilitic skin lesions resembling, (1941-2) 403
 - treatment,
 - Goeckerman's, (1944) 338
 - lipotropic substances, (1944) 338
 - vitamin D, (1940) 485
 - vitamin P, (1941-2) 362
 - X-ray, (1941-2) 362
 - wide-field, (1940) 104
- Psoriatic diathesis, (1944) 338
- Psychasthenia, hypnosis treatment in, (1939) 378
- Psychiatric syndromes, blast, and, (1943) 251
- Psychiatry, (1941-2) 79, (1943) 4, 314 *See also* Psychotherapy
 - advances in, (1940) 7
 - children, of, (1939) 497
 - behaviour disorders, (1939) 497
 - combined subjective and objective disorders, (1941-2) 362
 - encopresis, (1943) 314
 - food, excessive craving for, (1943) 314
 - industrial, (1943) 69, 365
 - reconstruction in, (1944) 343
 - research in, (1941-2) 83
 - war, in, (1941-2) 85, (1943) 66, 68, (1944) 78
- See also* Liffot syndrome
- Psychological factors,
 - asthma, in, (1944) 154
 - deafness, in, (1941-2) 201
 - effort syndrome, in, (1943) 231
 - night-blindness, in, (1943) 206
 - peptic ulcer, in, (1944) 318
 - skin diseases, in, (1939) 65
 - reactions in acne vulgaris, (1941-2) 128
 - tests, for aviators, (1941-2) 32
- Psychology, advances in, (1940) 7
- Psychoneuroses, (1939) 497, (1940) 485, (1941-2) 362, (1943) 314, (1944) 340-5
 - aetiology, (1941-2) 362
 - air-raids, civil reactions to, (1941-2) 363, (1944) 341
 - anxiety neurosis, cardiac disease, association with, (1944) 341
 - compulsion, leptazol therapy, (1941-2) 364
 - emotion syndrome, (1944) 340
 - evipan analysis in, (1941-2) 259
 - experimental observations, (1944) 344
 - eye, diseases and, (1944) 340
 - fever, neurogenic, (1944) 346
 - Forces, in, (1944) 340-5
 - habit formation, influence of faulty, (1944) 75
 - heredity in, (1943) 65

CUMULATIVE INDEX

Psychoneuroses—*continued*

- hypnosis in investigation of, (1941-2) 259
- obsessive-compulsion, leptazol therapy, (1941-2) 364
- ophthalmic disease, association with, (1944) 340
- prevention of, (1944) 75
- psychotherapy, and, (1939) 497
- adolescent neuroses, (1939) 497
- anxiety states, prognosis of, (1939) 497
- gastro-intestinal disturbances, relation to, (1939) 498
- stage fright, (1939) 497
- survey of, (1939) 22
- ulcerative colitis, in, (1939) 288
- recruits, in, (1944) 340
- traumatic experiences, reactions to, (1941-2) 363
- treatment of, (1940) 7
- war, in, (1940) 61
 - air-raids, effects of, (1944) 341
 - civilians and war injuries, (1944) 343
 - incidence in, (1944) 342-5
 - influence of, (1941-2) 85, 363
 - predisposition in, (1944) 344
 - psychopathic disposition, (1944) 342
 - treatment, (1943) 68, (1944) 343
- Psychopathic disposition, (1944) 342
- disturbances,
 - whooping-cough, in, (1944) 407
- personality, leucocytosis in, (1943) 315
- passive or inadequate type, (1944) 346
- war neuroses and, (1944) 342
- Psychopathology, (1944) 77
- choice of symptoms and, (1944) 297
- psychotherapy and, (1941-2) 83
- Psychoses,
 - affective, (1939) 498, (1941-2) 364, (1944) 346
 - aetiology, (1941-2) 364
 - bile acids and vitamin B₁ treatment, (1939) 499
 - depressive and manic, (1940) 487
 - diabetes mellitus, relation to, (1939) 498
 - hyperthyroidism in, (1943) 316
 - involutional-depressive, (1940) 488
 - involutional melancholia, (1940) 488
 - sex hormones, role of, (1941-2) 364
 - soldiers, in, (1943) 316
 - survey of, (1939) 118
 - treatment, (1940) 57-9, (1941-2) 365
 - convulsion therapy, (1940) 57
 - endocrines, (1941-2) 365
 - insulin shock, (1939) 118, 498
 - leptazol, (1943) 317
 - non-convulsant, (1941-2) 365
 - prefrontal leucotomy, (1943) 316
 - pre-frontal lobectomy, (1940) 72
 - prefrontal lobotomy, (1941-2) 365
 - sub-convulsant, (1941-2) 365
- alcoholic, (1939) 505, (1940) 497, (1941-2) 369
- cerebrospinal fluid pressure in, (1941-2) 188
- Korsakow's syndrome vitamin B₁ in, (1939) 506
- types and aetiology, (1939) 505
- biochemical research, (1940) 54
- cerebrospinal fluid pressure in, (1941-2) 188
- drugs, use of, (1944) 76
- electroencephalography in, (1944) 79
- experimental, mescaline, in, (1940) 54, 496
- Forces, in, (1944) 79
- intelligence tests in, (1944) 78
- involutional, endocrines in, (1944) 347
- liver function in, (1940) 54
- management in practice, (1944) 76
- manic-depressive,
 - aetiology, (1944) 346
 - cardiazol in, (1940) 487
 - curare in convulsion therapy, (1944) 346
 - hostility, role in causation, (1944) 346
- observation wards, (1944) 76
- parathyroid tetany complicated by, (1941-2) 322
- physiological research, (1940) 54
- pre-senile and senile, (1939) 506, (1944) 350
- Pick's disease, (1939) 506
- puerperal, progesterone treatment, (1944) 352
- pulmonary tuberculosis and, (1940) 391

Psychoses *continued*

- schizophrenia, (1939) 499
- aetiology and prognosis, (1939) 499
- diabetes complicating, (1943) 317
- treatment,
 - cardiazol and its dangers, (1939) 499, 504
 - histamine phosphate in, (1939) 503
 - insulin shock, (1939) 116, 503
 - magnesium sulphate-leptazol, (1943) 317
 - picriotoxin convulsion, (1939) 502
 - triazol convulsion, (1939) 502
- senile. *See* Psychoses, presenile and senile *supra*
- toxic infective, (1939) 505, (1944) 350
- bromide intoxication, (1939) 505
- carbon disulphide poisoning causing, (1943) 365
- Kleime-Levin syndrome, (1943) 318
- thiocyanates causing, (1943) 318
- traumatic, (1941-2) 363
- treatment,
 - electrical convulsion, (1944) 351
 - general hospitals, in, (1944) 350
 - refrigeration, (1944) 351
- Psychosomatic medicine, (1940) 7, (1944) 79
- Psychotherapy, (1940) 486, (1941-2) 362, (1944) 340-5
 - alcoholism, in, (1944) 123
 - experimental observations, (1944) 344
 - frontal leucotomy, (1943) 67, 316
 - group, (1944) 74
 - menopausal symptoms, in, (1941-2) 191
 - psychopathology and, (1941-2) 83
 - rehabilitation, for, (1943) 315
 - shock, (1943) 4, 66, 317
 - sodium amylal, use of, (1944) 344
 - stammering, (1944) 377
 - war neuroses, acute, in, (1944) 343
- Ptosis, monocular, in myasthenia gravis, (1943) 284
- Public health, (1944) 351 *See also* Infective diseases
- war, in, (1944) 1
 - air-raid precautions, (1944) 8
 - day nurseries, (1944) 8
 - diseases in present war, (1944) 9
 - early plans, (1944) 2
 - emergency medical service, (1944) 3
 - evacuation scheme, (1944) 6
 - history, (1944) 1
 - housing and accommodation, (1944) 8
 - industrial health, (1944) 9
 - outbreak of present war, (1944) 2
 - preliminary work in war organization, (1944) 3
- Public Health Acts, (1939) 6
- Puerperal sepsis, (1940) 499
- aetiology, (1940) 499
- history, (1944) 353
- streptococcus, haemolytic, (1940) 499
- treatment,
 - chemotherapy, specific, (1944) 353
 - sulphanilamide, (1940) 499
 - sulphonamides, (1941-2) 370
- Puerperium, (1939) 507, (1941-2) 370, (1944) 352-5
- after-pains, (1940) 497
- mechanical recording of contractions, (1944) 352
- breast,
 - abscess, acute, (1944) 166
 - engorgement, (1940) 497
 - methyl testosterone, early use of, (1944) 352
- cerebral thrombophlebitis in, (1943) 318
- complications, (1940) 498, (1944) 352
- diet in, (1944) 142-5
- embolism and thrombosis in, (1944) 280
- ergometrine in, (1941-2) 370
- haemoglobin levels in, (1944) 23
- hypophyseal necrosis, acute, (1940) 465
- insanity complicating, (1939) 507
- progesterone treatment, (1944) 352
- intracranial venous thrombosis in, (1939) 4
- lactation, inhibition of, (1940) 500
- oestrim, by, (1939) 508
- management of, (1944) 353
- normal, management of, (1940) 497, (1941-2) 370
- physiology, (1941-2) 370

CUMULATIVE INDEX

Puerperium—continued

- psychosis in, progesterone treatment, (1944) 352
- prophylaxis, (1939) 507
- sulphonamides in treatment, (1939) 17, 31, 507
- survey of, (1939) 31
- puerperal sepsis, (1939) 507
- Cl. welchii* infection, sulphanilamide treatment of, (1939) 507
- purpura rheumatica in, (1940) 498
- sterilization in, (1941-2) 22
- testosterone propionate in, (1940) 497, 500
- thrombosis of cerebral veins in, (1941-2) 407
- urinary suppression, post-partum, (1940) 499
- uterus,
 - eigot in promoting involution, effect of, (1944) 23
 - inversion, (1944) 280
 - acute, (1940) 498
 - posterior pituitary extracts, response to, (1940) 498
 - stilboestrol, effect of, on, (1941-2) 370
- Pulmonary
 - artery,
 - aneurysm of, (1939) 214, (1941-2) 144 *See also* Aneurysm
 - aortic aneurysm rupturing into, (1943) 122
 - embolism, effect of post-operative graduated exercises on death-rate from, (1939) 33
 - circulation, eupaverin, effects of, (1940) 451
 - embolism *See also* Embolism
 - amniotic fluid causing, (1943) 261
 - causes and prevention of, (1944) 15
 - fat, (1943) 2
 - emphysema, cor pulmonale, relation to, (1943) 240
 - eosinophilia, (1941-2) 157
 - osteoarthritis, (1941-2) 274, (1944) 276
 - hypertrophic, (1939) 390
 - plexus, resection of posterior, in asthma, (1939) 232
 - stenosis, aortic aneurysm and, (1941-2) 143
 - tuberculosis *See* Tuberculosis, pulmonary
 - tularaemia, (1943) 369
 - Pulse, response test, (1941-2) 244
 - Puncture of posterior fornix, needle, (1940) 23
 - Pupil
 - atropine, scopolamine, and homatropine-pare-drine, effects of, (1940) 449
 - catatonic, (1944) 348
 - Purgatives, abuse of, clinical entity caused by, (1939) 50
 - Purpura
 - anaphylactic, regional ileitis simulated by, (1943) 180
 - haemorrhagic (Werthof's disease), (1939) 547
 - arsenical therapy causing, (1940) 325
 - arsphenamines causing, (1941-2) 213
 - meningococcal septicaemia associated with, (1941-2) 186
 - rheumatica, puerperium, in, (1940) 498
 - rheumatism associated with, (1941-2) 241
 - simplex, familial, rheumatism associated with, (1941-2) 241
 - thrombocytopenic *See also* Thrombocytopenic purpura
 - aetiology, diagnosis and treatment, (1941-2) 241
 - measles complicated by, (1941-2) 302
 - sulphapyridine causing, (1941-2) 343
 - unsolved problems in, (1940) 6
 - vitamin C deficiency cause of, (1939) 14
 - treatment,
 - parathyroid, (1941-2) 241
 - vitamin P, (1940) 130, (1941-2) 241
 - Pus, aseptic, wounds treated with, (1940) 349
 - Pyelectan, iodoxyol, official name for, (1940) 127
 - Pyelitis, (1939) 508
 - adrenal cortex and bone marrow treatment, (1939) 508
 - B. coli*, sulphonamide treatment of, (1939) 17, 41
 - mandelic acid and sulphanilamide in, (1939) 159
 - pregnancy, of, (1940) 480, (1941-2) 19
 - morbid anatomy of, (1939) 509
 - sulphanilamide in, (1939) 508; (1940) 501

Pyelitis—continued

- sulphathiazole and sulphamethylthiazole in, (1940) 501
- sulphonamides in, (1939) 17
- Pyelography
 - excretion, uroselectan B in, (1941-2) 371
 - intravenous, in prostatic disease, (1941-2) 360
 - pyelo-renal backflow, (1943) 322
 - urogram, delayed, (1940) 370
- Pyelonephritis
 - hydrocele renis associated with, (1943) 258
 - hypertension and, (1940) 212, (1941-2) 165, (1944) 310
 - mercurochrome in, (1939) 384
 - unilateral atrophic, and malignant hypertension, (1941-2) 165
- Pyelo-renal backflow, (1943) 322
- Pyelo-ureteral dilatation, hormones producing, (1943) 19
- Pylephlebitis
 - diagnosis, thorium dioxide in, (1941-2) 288
 - sulphonamides in, (1940) 12
- Pyloric
 - hypertrophic stenosis, (1939) 509, (1940) 501
 - heredity, (1939) 509
 - obstruction, (1939) 509
 - treatment, eumydrin, (1939) 509, (1941-2) 370
 - obstruction, (1940) 501, (1941-2) 370
 - stenosis,
 - acidosis associated with, (1941-2) 128
 - blood changes in, (1941-2) 128
 - congenital,
 - atropine methylnitrate (eumydrin) in, (1939) 165
 - operative treatment of, (1941-2) 13
 - eumydrin, in, (1940) 502, (1941-2) 4, 50
- Pyoderma, mental deficiency associated with, (1939) 411
- Pyorrhoea alveolaris, gastric disorders, relation to, (1944) 31
- Pyramidal
 - hypertonia, haematopoehyphyrin in, (1940) 415
 - tract, lesions, 'finger reflex' in, (1940) 508
- Pyrethrum, dermatitis caused by, (1941-2) 202
- Pyretotherapy
 - asthma, in, (1940) 161
 - autohaemotherapy and, in arthritis, (1940) 201
 - cerebral haemodynamics in, (1940) 299
 - choleca, in, (1941-2) 189
 - complications, (1940) 202
 - disseminated sclerosis, in, (1941-2) 212
 - endocarditis, subacute bacterial, in, (1940) 335
 - general paralysis of insane, in, (1941-2) 315
 - general paresis, in, (1941-2) 105
 - gonorrhoea, in, (1940) 319, (1941-2) 238, (1944) 243
 - herpes caused by, (1940) 202
 - keratosis blenorrhagica, (1940) 321
 - malignant disease treated by irradiation and, (1944) 175
 - nausea and vomiting caused by, (1940) 202
 - rheumatoid arthritis, in, (1940) 199
 - sulphonamides with, (1941-2) 108
 - syphilis, in, (1943) 90
- Pyrexia
 - artificial, abortion caused by, (1944) 120
 - obscure, (1939) 510, (1940) 502
 - neurogenic hyperthermia, (1939) 510
 - post-operative, (1940) 502
 - recurrent, and migraine, (1944) 346
 - sulphonamides cause of, (1939) 176
- Pyridine
 - epilepsy treated with, (1944) 229
 - hepato-renal disease caused by, (1944) 229
- Pyridoxin, (1941-2) 5, 423 *See also* Vitamin B₆
- hydrochloride *See* Vitamin B₆
- Pyrogen-free water, intravenous transfusion, for, (1940) 356
- Pyruvic acid, blood, in, (1940) 114
- Pyuria
 - children, in, (1941-2) 418
 - chronic, congenital anomalies of urinary tract and, (1941-2) 231
 - sterile, in urinary tuberculosis, (1940) 365

CUMULATIVE INDEX

Q

- Q fever, (1939) 81
actiology, (1939) 81
clinical picture, (1939) 81
diagnosis and differential diagnosis, (1939) 84
Rickettsia burnetti cause of, (1939) 81
treatment, (1939) 85
 Quartz-rod transillumination, intrahepatic circulation observed by, (1941-2) 288
 Quinacrine, mepacrine hydrochloride, official name for, (1940) 127
 Quinidine
 arrhythmia treated with, (1939) 59
 auricular standstill and, (1940) 192
 tachycardia, in, (1939) 223
 Quinine
 alternatives to, (1943) 82
 bihydrochloride, malaria treated with, (1943) 277
 deafness in relation to, (1939) 297
 dihydrochloride and urethane, hydrocele treated by injections of, (1943) 360
 dystonia musculorum delormans, in, (1939) 438
 fat in body, (1939) 467
 insulin, and, mixture, diabetes mellitus treated with, (1941-2) 207
 malaria, in, (1939) 144, (1940) 75, 400
 myotonia congenita (Thomsen's disease), in, (1939) 166, 437
 paralysis agitans, in, (1941-2) 322
 poisoning, (1940) 559
 supply of, (1943) 278
 urethane, and, (1941-2) 112
 Quinocaine, in staphylococcal infection, (1941-2) 339
 Quinoline acid, pellagra treated with, (1940) 436

R

- Rabbit thrombin, local haemostatic, as, (1943) 118
 Radioactive phosphorus
 cancer treated with, (1943) 171
 leukaemia, effects in, (1943) 265
 Radio-dermatitis, surgical treatment of, (1941-2) 202
 Radiographic examination. *See* X-ray examination
 Radiography. *See also* X-ray examination
 asthma, in, (1939) 231
 chest, of, (1939) 113
 contrast, (1943) 321
 examination. *See* X-ray examination
 mass, (1941-2) 75, (1943) 2, 319, 324. *See also*
 Mass radiography, X-ray examination
 Air Training Corps, in, (1943) 319
 American Navy, in, (1943) 320
 factory workers, in, (1943) 320
 industry, in, (1943) 320
 mass miniature,
 Australian children, in, (1944) 356
 technique, (1944) 357
 pulmonary tuberculosis, in, (1940) 6
 recruits, in, (1943) 319
 Royal Air Force, in, (1943) 319
 Radio-humeral bursitis, sodium mouhuate therapy, (1940) 300
 Radiology, (1940) 502-6, (1941-2) 371, (1943) 319
 See also Radiotherapy, Radium therapy
 X-ray examination, X-ray therapy
 cardiovascular diseases, in, (1940) 5
 diagnosis and treatment, in, (1939) 511
 arteriography, (1939) 512
 bronchography, (1939) 512
 contrast cystogram, (1939) 513
 encephalography, (1939) 513
 myelography, (1939) 513
 radiocardiography, (1939) 59
 radon gas,
 skin lesions, in, (1939) 514
 skiodan (sodium monoorodmethanesulphonate) as contrast medium, (1939) 511
 surgery, in, (1939) 23
 thorium dioxide as contrast medium, (1939) 511
 tomography, (1939) 512
 ventriculography, (1939) 513
 Radioneurotic ulcers, zinc treatment, (1941-2) 372
 Radiophotography, (1940) 103

- Radiotherapy, (1940) 104, 504-6, (1941-2) 372; (1943) 323, (1944) 358
 bladder, carcinoma of, in, (1943) 144
 breast, carcinoma of, in, (1941-2) 176
 bronchial carcinoma, in, (1944) 69
 cancer, in, (1940) 242, 504; (1941-2) 184, (1944) 175
 pharynx and larynx, of, (1939) 90
 post-operative, (1944) 175
 quantitative examination of biopsy material in, (1941-2) 184
 surrounding tissue, treatment of, (1941-2) 185
 carbuncle and furuncle, in, (1939) 516
 carcinoma, superficial, in, (1939) 517
 Chaul technique of, (1939) 516
 clinical application, (1941-2) 373
 endocrine gland, in, rash after, (1939) 516
 glaucoma, in, (1940) 313
 granuloma, in, (1939) 514
 Grenz rays,
 eye disease, in, (1939) 517
 skin disease, in, (1939) 517
 inflammation, in, (1939) 515
 irradiation of entire body, (1944) 358
 lobar pneumonia and broncho-pneumonia, in, (1939) 514
 malignant disease, in, (1941-2) 184
 mastitis, chronic interstitial, in, (1940) 104
 oriental sore, in, (1944) 284
 ovarian tissue, resistance to, (1939) 516
 parotid gland tumours, in, (1943) 299
 radioneurotic ulcers, zinc treatment, (1941-2) 372
 skin,
 cancer, in, (1943) 344
 disease, in, (1941-2) 373
 injuries, in, (1939) 514
 survey of, (1939) 18
 uterine fibromyomas, in, (1941-2) 419
 wounds, effect on, (1939) 515
 Radium, poisoning by, (1940) 563
 Radium therapy, (1941-2) 373
 angioma, in, (1939) 218, (1940) 186
 birth-marks, for, (1941-2) 373
 cancer, in, (1939) 28, 272, (1940) 242, 504
 carcinoma,
 breast, of, (1940) 232, (1941-2) 176
 cervix uteri, of, (1941-2) 419, (1943) 20
 cheek, of, (1940) 504
 penis, of, (1941-2) 325
 vagina, of, (1944) 358
 clinical applications, (1941-2) 373
 comparative effects of radon and, (1940) 505
 glaucoma, in, (1940) 313
 injuries from, (1943) 323
 interstitial, in carcinoma of cervix, (1940) 578
 kerato-iritis, tuberculous, beta-rays in, (1940) 579
 metrorrhagia, (1944) 303
 parotid gland tumours, in, (1943) 299
 parotitis, post-operative, in, (1943) 299
 plantar warts, in, (1941-2) 393
 post-irradiation necrosis, (1943) 323
 Riedel's thyroiditis, in, (1939) 355
 Radius, dislocation of head of, fracture of ulna associated with, (1940) 276
 Radon
 comparative effects of radium and, (1940) 505
 tongue, black hairy, treated with, (1940) 411
 Ragweed pollen in asthma, (1939) 200
 Rammstedt's operation, (1941-2) 13
 Rash, sulphonomides causing, (1939) 176, (1941-2) 344
 Raspberry leaves, relief of dysmenorrhoea and labour pains with, (1941-2) 20, (1943) 96
 Rat-bite fever
 fatal termination, (1941-2) 374
 neoisphenamine in, (1939) 147
 Raynaud's
 phenomenon, (1939) 518
 cold agglutination, spontaneous, in, (1943) 325
 morbid anatomy, (1939) 518
 papaverine, intravenous, (1939) 518
 parathyroidectomy, (1939) 518
 sclerodactyly (acroscclerosis), in, (1941-2) 374
 scleroderma and pulmonary fibrosis in, (1941-2) 375

CUMULATIVE INDEX

Raynaud's—continued

- syndrome,
 - clinical picture, (1941-2) 374, (1944) 82
 - treatment, (1944) 82
- Recklinghausen's disease, (1943) 291
- Recruits
 - albuminuria in, (1943) 110
 - cardiac examination of, (1940) 329-31
 - cardiovascular diseases in, (1941-2) 44
 - effort syndrome and, (1943) 231
 - examination of, (1941-2) 44
 - heart disease in, (1941-2) 244
 - heart of, (1941-2) 2
 - mass radiography in, (1940) 104, (1943) 319
 - psychoneuroses in, (1944) 340
 - radiography, miniature film, in, (1940) 94
- Rectal
 - administration,
 - drugs, of, absorption and excretion, (1941-2) 339
 - nutrients and drugs, of, (1944) 327
 - sulphanilamide, of, (1941-2) 343
 - anaesthesia, (1943) 121
 - incontinence, treatment, surgical repair of sphincter ani, (1944) 359
 - surgery, (1941-2) 14
- Recto-vaginal septum, endometriosis of, (1941-2) 221
- Rectum
 - absorption of nutrients and drugs, (1944) 327
 - diseases, (1939) 519, (1940) 506, (1941-2) 375, (1944) 359
 - amoebic granuloma,
 - Balantidium coli* infection, and, (1940) 167
 - simulating carcinoma, (1940) 167
 - carcinoma,
 - diagnosis and treatment of, (1939) 519
 - perineal colostomy, (1940) 507
 - radiotherapy in, (1940) 507
 - X-ray treatment without colostomy, (1941-2) 375
 - endometriosis, (1939) 519
 - drugs administered per, (1941-2) 339
 - haemorrhage, heterotopic gastric mucosa causing, (1940) 279
 - nutrients and drugs administered per, (1944) 327
 - polyp, (1940) 506
 - polyposis, differential diagnosis, (1941-2) 375
 - precursor of carcinoma, (1941-2) 375
 - simple ulcers of, (1941-2) 193
 - sulphanilamide administered per, (1941-2) 343
 - surgery of, (1941-2) 14
 - tumours,
 - benign, (1941-2) 375
 - injection of piles, after, (1940) 506
 - carcinoid, (1944) 359
 - malignant, (1941-2) 375
- Rectus abdominis muscle, spontaneous haemorrhage into, (1940) 413, (1943) 282
- Red cell fragility, Creed's test for, (1939) 52
- Red hair, and susceptibility to tuberculosis, (1941-2) 414
- Redlich-Fischer plaques, (1943) 113
- Reflex
 - carotid sinus, in coronary disease, (1943) 126
 - draught, (1944) 262
 - feeding, in new-born, (1944) 262
- Reflexes, (1940) 507
 - Babinski's, (1941-2) 376
 - bridge-of-nose eyelid reflex, (1940) 508
 - crossed plantar responses, (1941-2) 376
 - diagnosis, in, (1939) 520, (1941-2) 376
 - finger reflex, pyramidal tract lesions, (1940) 508
 - knee-jerk, new method of eliciting, (1939) 520
 - plantar reflex, (1939) 521
 - shoulder girdle, idio-reflex of, (1939) 520
 - fundus oculi, of, (1941-2) 227
 - tendon-jerks, absence of, (1940) 507
- Refraction
 - cycloplegia, drugs used for production of, (1940) 508
 - practical methods, (1939) 521
 - homatropine and benzedrine as mydriatic, (1939) 521

Refrigeration

- anaesthesia induced by, (1943) 114
- cancer treated by, (1941-2) 184, 350
- crush syndrome, effect on, (1944) 273
- general and local, (1941-2) 350
- local, in treatment of carcinoma of cervix uteri, (1941-2) 419
- morphine addiction treated by, (1941-2) 350
- psychoses treated by, (1944) 351
- Regional
 - ileitis. *See* Crohn's disease
 - X-ray baths, (1940) 105
- Regulation 33 B, (1944) 10, 102
- Rehabilitation, (1941-2) 8
 - centres, (1943) 10
 - coronary occlusion, after, (1941-2) 146
 - fractures, after, (1943) 196
 - head injuries, after, (1943) 178
 - industry, in, (1944) 360
 - psychoneuroses, in, (1943) 315
 - psychotherapy and, (1943) 315
 - tuberculosis, in, (1944) 291
- Relapsing fevers
 - neorarsphenamine in, (1939) 147
 - tick relapsing fever (non-epidemic), (1943) 325
- Renal
 - aneurysm, rupture during pregnancy, (1944) 25
 - calculus. *See* Calculus
 - carbuncle, (1943) 259
 - colic, sulphonamides causing, (1941-2) 116, 346
 - complications,
 - sulphadiazine causing, (1944) 328
 - sulphonamide therapy causing, (1941-2) 343, (1944) 245
 - diseases. *See* Kidney, diseases
 - dysfunction, in prostaticism, (1943) 313
 - extract, hypertension, in, (1941-2) 166, (1943) 149
 - failure, crush injuries, in, (1941-2) 269, (1943) 249
 - function test, one-hour renal condition test, (1940) 575
 - hypertension, (1941-2) 165
 - insufficiency,
 - blood transfusion causing, (1941-2) 170
 - peritonitis nodosa and, (1944) 150
 - prolonged, complicating hyperparathyroidism, (1941-2) 323
 - ischaemia and hypertension, (1941-2) 2
 - lesions,
 - crush syndrome in, (1943) 249
 - diabetes mellitus, in, (1943) 288
 - eclampsia, in, (1944) 24
 - Papilla,
 - angioma in, (1943) 229
 - lesions of, causing haematuria, (1943) 229
 - reactions in cholera, (1943) 174
 - tuberculosis, spontaneous healing in, (1943) 259
- Rendu-Osler syndrome, (1941-2) 223
- Remin
 - eclampsia, and, (1941-2) 18
 - hypertension, role in, (1941-2) 165
 - nephrectomy on pressor response to, effect of, (1941-2) 166
- Reno-ureteral disease, reflex abdominal pain and (1944) 119
- Reparative or restorative surgery, (1941-2) 12
- Research in medicine, future of, (1940) 7, 8
- Respiration
 - artificial, (1941-2) 212
 - foetal sheep, in, (1944) 330
 - heart disease, in, effect of coramine on, (1941-2) 334
 - pentothal sodium and, (1940) 177
 - physiology, in relation to anaesthesia, (1940) 172
 - pneumectomy, effects of, (1944) 295
- Respirator dermatitis, (1943) 182
- Respiratory
 - diseases, (1941-2) *See also* Pneumonia, Tuberculosis, pulmonary
 - asthma, (1943) 2
 - fat embolism, (1943) 2, 337
 - treatment, recent advances, (1943) 272
 - function tests, (1943) 58
 - infections, positive syphilitic reactions in, (1943) 88

CUMULATIVE INDEX

- Respiratory—continued**
tract,
diseases,
advances in knowledge of, (1940) 6
allergic, (1940) 160
Hodgkin's, (1941-2) 258
hyperplastic disease and allergy, (1940) 160
tonsillectomy, effects of, (1944) 168
infections, irradiation of air and, (1940) 150
upper,
infections of, in relation to asthma, (1941-2) 157
streptococcal infections and rheumatic fever, (1941-2) 377
- Rest**
pulmonary tuberculosis, in, (1939) 114
rheumatism, in, (1939) 140
- Resuscitation**, (1939) 521
atropine-adrenaline-strophanthin mixture, use of, (1940) 509
cardiac arrest, in, (1943) 326
drowning, in, (1941-2) 212
mechanical respiration, (1939) 521
oxygen administration apparatus, (1939) 521
- Reticulo-endothelial cytomycosis**, (1943) 243
Reticulo-endotheliosis of spleen, (1939) 547
Reticulogen in ulcerative colitis, (1939) 286
- Retina**
angioma, X-ray therapy, (1940) 385
angiomatosis, treated by catholysis and surface diathermy, (1941-2) 377
arterial spasm, pregnancy toxæmia, in, (1940) 18
artery, central, post-partum obstruction of, and hemiplegia, (1940) 510
degenerations of, (1941-2) 162
detachment,
aetiology, (1941-2) 377
surgical treatment, (1941-2) 377
disease, (1939) 522, (1940) 510, (1941-2) 376
detachment of, (1939) 130
diagnosis, vital staining in, (1939) 522
leukaemia cause of changes in, (1939) 404
retinitis proliferans, (1939) 522
tumour, (1939) 523
vascular, (1939) 522
glioma of, (1943) 326
haemorrhage, tick-bite fever, and, (1940) 84
blood transfusion, after, (1943) 326
diabetes mellitus, in, (1943) 186
phakomias of, (1943) 204
retinoblastomas and neuro-epitheliomas, of, (1943) 326
tumours, (1941-2) 377
varices, in diabetic retinitis, (1941-2) 376
vascular diseases, (1940) 510, (1941-2) 376
venous thrombosis, treated by heparin, (1941-2) 376
- Retinal spasm, pregnancy toxæmia, in**, (1940) 18
- Retinitis**
diabetic, varices in, (1941-2) 376
exudative, (1940) 510
pigmentosa, (1941-2) 376
atropine sulphate, treatment with, (1941-2) 376
clinical picture, (1941-2) 376
- Retinoblastomas**, (1943) 326
Retio-pyelography, (1943) 322
- Rhabdomyoma of larynx**, (1943) 41
Rhabdomyosarcoma of orbit, (1943) 147
Rhabdomyosarcoma of prostate, (1940) 484
Rhagades, of congenital syphilis, (1941-2) 403
- Rhesus factor**
blood transfusion, in, (1943) 3, 29, 148
erythroblastosis foetalis, in, (1943) 3, 16, 24, 119
racial incidence, (1944) 159
- Rheumatic**
endocarditis, (1943) 327
fever *See also* Rheumatic infection, acute
acute, in old age, (1941-2) 380
aetiology of, (1940) 5
appendicitis, acute, associated with, (1941-2) 377
heart lesions, (1940) 332
mitral stenosis after, (1940) 336
prophylactic treatment by sulphanilamide, (1943) 327
- Rheumatic—continued**
fever—*continued*
streptococcal upper respiratory infection and, (1941-2) 377
sulphonamides in treatment, (1941-2) 49
heart disease, (1940) 332. *See also* Heart infection,
prophylactic treatment with sulphanilamide, (1941-2) 378
recurrence in streptococcal upper respiratory infection, (1941-2) 377
treatment, (1941-2) 378
infection, acute, (1939) 135, 523, (1941-2) 377; (1944) 360-2
aetiology, (1939) 136, 523; (1940) 510, (1944) 360
antistreptolysin titre in serums, (1940) 511
bacteriology, (1940) 511
morbid anatomy, and, (1941-2) 377
cardiac lesion, (1941-2) 377
children, in, (1941-2) 377
association with acute appendicitis, (1941-2) 377
class incidence, (1944) 360
classification, (1939) 135
clinical picture, (1940) 511, (1941-2) 377
cutaneous eruption, (1940) 511
diagnosis, (1944) 361
two-step test, (1941-2) 378
German measles, in, (1940) 312
haemolytic streptococci, recovery of, (1941-2) 377
pathology, (1939) 138
prognosis by blood picture, (1943) 327
recurrence, prevention by chemotherapy, (1944) 362
statistical survey, (1944) 360
symptoms and signs, (1939) 136, (1944) 361
treatment, (1939) 139
chemotherapy, (1944) 362
convalescent serum, (1940) 511
sulphanilamide, (1939) 523
Tropics, in the, (1940) 510
inflammation, myocvites in, (1943) 327
nodule, pathology of, (1939) 138
pericarditis, salicylate therapy, (1941-2) 248
- Rheumatism**, (1943) 208. *See also* Fibrositis, Rheumatoid arthritis
aconitine ionization in, (1939) 326
chronic, unsolved problems of, (1940) 7
formol-gel reaction in diagnosis, (1941-2) 154
gout, relation to, (1940) 321
hydrotherapy in, (1939) 376
juvenile. *See* Rheumatic infection, acute
muscular, (1941-2) 229
old age, in, (1941-2) 229, 381
palindromic, (1943) 112
purpura associated with, (1941-2) 241
skin disease, relation to, (1939) 65
treatment,
heat and Scott's dressing, (1941-2) 229
physical methods, (1941-2) 229
- Rheumatoid arthritis**, (1939) 226
acute rheumatism, relation to, (1939) 135
aetiology, (1940) 198, (1941-2) 153, (1944) 152
aspiration of joint effusions in, (1940) 200
cardiac lesions in, (1941-2) 154
cinchophen in, (1939) 227
colonic infection in, (1944) 152
diagnosis, (1941-2) 154
formol-gel reaction in, (1941-2) 154
vital azo dye in, (1939) 226
extra-articular lesions, (1941-2) 154
facies and personality in, (1943) 136
Felty's syndrome, (1944) 152
focal infection and, (1941-2) 154
heart disease associated with, (1941-2) 154
morbid anatomy, (1944) 152
necrocleritis nodosa associated with, (1940) 254
nerve lesions, histology of, (1944) 152
pathology and prognosis, (1944) 152
Pseudomonas pyocyanea infection and, (1944) 152
psychological approach to, (1943) 136
sulphur metabolism in, (1940) 198

CUMULATIVE INDEX

Rheumatoid arthritis—continued

- treatment, (1940) 198
- artificial fever, (1940) 199
- bee venom in, (1940) 198; (1941–2) 155
- chrysotherapy, (1940) 198, (1941–2) 154, (1943) 137, (1944) 153
- histamine, (1940) 198
- jaundice, therapeutic, (1939) 227
- parmanil, (1939) 226
- splenectomy, (1940) 199
- splints and physiotherapy, (1941–2) 154
- sulphur,
 - colloidal, (1940) 198
 - iodine, and, (1939) 227
 - vitamin A deficiency in, (1941–2) 153
 - vitamin C in, (1940) 198
 - vitamin D in, (1939) 227
- X-rays, high voltage, (1941–2) 373
- Rhinitis
 - atrophic, (1939) 90
 - treatment,
 - hormone therapy, (1944) 53
 - oestrogens, in, (1944) 314
 - chronic obstructive,
 - sodium morrhuate injections, (1941–2) 317
 - submucosal injections of sodium psyllate, (1941–2) 317
 - vasomotor, (1940) 162, (1944) 126
- Rhinology, (1939) 90
- Rhinorrhoea, cerebrospinal, bifrontal craniotomy for, (1941–2) 188
- Rhinoscleroma
 - Mikulicz's cells in, (1943) 328
 - telerradiumtherapy, effects of, (1940) 512
- Rhinosporidiosis, (1939) 524
- eye,
 - infection of, (1939) 524
 - lesions in, (1940) 512
- Rhipucephalus appendiculatus*, vector of tick-bite fever, (1940) 81
- Rib, cervical, (1941–2) 189
- Riboflavin, (1940) 115 *See also* Vitamin B₂
 - administration in diabetes mellitus, (1941–2) 206
 - deficiency and pantothenic acid, (1941–2) 424
 - rosacea keratitis, in, (1940) 254
- Ricinoic acid, (1943) 96
- Rickets, (1939) 524
 - acidosis and late, (1944) 362
 - adult, cataract associated with, (1941–2) 186
 - calciferol in prevention and treatment, (1940) 513
 - citric acid and sodium citrate in treatment, (1939) 525
 - deficiency disease, as a, (1940) 4
 - late, acidosis, relation to, (1944) 362
 - milk and, (1940) 346
 - pathogenesis and morbid anatomy, (1944) 362
 - prevention, (1939) 524
 - war-time, in, (1943) 328
 - vitamin D₁, action of, (1939) 524
 - vitamin D in, (1940) 130, 589
 - vitamin-resistant, (1939) 525
 - vitamins in relation to, (1939) 38
- Rickettsia*
 - antigenic types, (1944) 394
 - infections, (1940) 4
 - tick-bite fever caused by, (1940) 80
 - tsutsugamusho ictanalis* virus, in treatment of general paralysis of the insane, (1940) 60, 425
 - vaccines in typhus fevers, (1940) 76–8
- Rickettsial diseases, Australia, in, (1944) 394
- Ringworm, (1939) 342 *See also* Fungous diseases
 - feet, of, (1943) 218
 - feet and hands, of, preventive treatment, (1941–2) 233
 - footwear as source of, (1943) 218
 - scalp, of, gentian violet treatment, (1940) 304
 - treatment,
 - iontophoresis of copper sulphate, (1943) 217
 - trichophytin in, (1943) 218
- Ritter's disease
 - aetiology and treatment of, (1943) 184
 - sulphapyridine in, (1940) 260
- Rivers's culture virus, vaccination, for, (1940) 579

Rodent ulcer

- recurrence, persistent, treatment of, (1943) 346
- unusual sites, (1943) 346
- Rodilone, (1940) 134
- Roentgen cinematography, cardiac circulation, of, (1944) 355
- Rorschach test, (1941–2) 85
- Rose hips, source of vitamin C, (1943) 95
- Rotating
 - hexagon for-testing night-vision, (1941–2) 31
 - stereogram, (1941–2) 31
- Rotenone, scabies treated with, (1940) 531, (1941–2) 391, (1943) 343
- Royal Air Force, mass radiography in, (1943) 319
- Rubber dermatitis, (1943) 182
- Rubiazol, (1940) 133
 - chemistry of, (1939) 170
 - lupus erythematosus treated with, (1940) 396
- Rubus idaeus*, extract of, (1941–2) 20
- Rud's syndrome, (1939) 379
- Rupial syphilis, (1940) 548
- Rupture
 - duodenum, of, (1943) 250
 - peptic ulcer, of, (1943) 11
 - urethra, of, (1943) 372
- Russell's viper venom, use in estimation of thrombo-kinase, (1941–2) 163

S

- Saccharin, use of in war-time, (1940) 453
- Sacro-iliac strain, (1943) 142
- 'Safe' period, (1941–2) 197
- fertility and, (1944) 379
- Salicylates, rheumatic pericarditis treated with, (1941–2) 248
- Saligemin, neurosyphilis treated with, (1941–2) 316
- Saline
 - hypertonic,
 - artificial fever therapy, preceding, (1940) 202
 - bacillary dysentery treated with, (1944) 100
 - cholera treated with, (1944) 100
 - shock treated with, (1941–2) 388
 - intravenous, anuria treated with, (1943) 174
 - transfusion, (1940) 11
 - shock, in, (1941–2) 387
- Saliva, sulphapyridine, excretion in, (1940) 459
- Salivary
 - gland, diseases of, (1940) 513
 - tumours, (1943) 299, (1944) 304
 - histological classification, (1944) 362
 - mixed, (1944) 362
 - syndrome, premenstrual, (1940) 434
- Salmonella*
 - actincke*, food poisoning caused by, (1944) 235
 - infections, recent work on, (1944) 60
 - septicaemia, (1944) 235
- Salpingitis, gonorrhoeal, oestrogenic therapy, (1941–2) 228
- Salt, Addison's disease treated with, (1940) 153
- Salt-free diet, Mènière's syndrome treated by, (1943) 377
- Salt-poor diet, pregnancy and labour, effect on, (1940) 371
- Salvarsan, and the history of synthetic chemo-therapy, (1940) 3
- Salyrgan, (1943) 1
 - oedema, in treatment of, (1940) 5
 - San Joaquin Valley fever, (1943) 146, 205
- Sand-blast, acute silicosis in, (1941–2) 389
- Sanocrysin
 - agranulocytosis caused by, (1940) 156
 - arthritis, in, (1940) 200
- Santonin poisoning, (1941–2) 408
- Saphenous vein, internal, removal of, (1940) 13
- Sarcoid
 - Besnier-Breck-Schaumann disease, (1943) 347
 - Boeck's, (1940) 533, (1941–2) 394. *See also* Boeck's sarcoid
 - clinical picture, (1944) 375
- Sarcoidosis, (1943) 347
 - bronchial, (1941–2) 295
 - erythema nodosum, relation to, (1943) 205

CUMULATIVE INDEX

Sarcoma

- breast, of*, (1940) 233
- diaphragm, rhabdomyosarcoma of, (1939) 310
- diet and, (1940) 240
- duodenum, leiomyosarcoma of, (1939) 388
- erythraemia associated with stem-celled, (1939) 336
- filter-passing virus causing, (1940) 7
- haematoma, arising from, (1941-2) 183
- interaction of sarcoma cells with leucocytes and macrophages, (1940) 569
- jejunum, of, (1941 2) 272
- Jensen's rat, X-ray therapy, (1941-2) 372
- Kaposi's pigmentary, (1943) 347, (1944) 374
- omentum, of, (1941-2) 329
- osteogenic, (1940) 227, (1943) 161
- popliteal space, of, (1940) 570
- stomach, of, (1943) 353
- trachea, of, (1940) 563
- uveal tract, of, (1941 2) 420
- Sarcomatous degeneration in neurofibromatosis, (1943) 291
- Sausages, outbreak of trichiniasis caused by, (1943) 366
- Scabies, (1941-2) 391
 - centres for treatment, (1943) 341
 - children, in, (1944) 372
 - civil and military problem, (1943) 343
 - mite, life history of, (1943) 340
 - pediculosis and, (1941-2) 391
 - sarcoptoides, evaluation of, (1943) 341
 - transmission, (1943) 341
 - treatment, (1941-2) 120, (1944) 117
 - benzyl benzoate, (1941-2) 391, (1943) 342, 348, (1944) 372
 - creolin, (1940) 531
 - derris root, (1941 2) 391
 - drugs, various, (1943) 342
 - emulsions, (1944) 372
 - rotenone, (1940) 531, (1941-2) 391, (1943) 343
 - soap containing sulphur, (1943) 343
 - sulphur, (1943) 342
 - tetraethylthiuram monosulphide, (1944) 117, 373
 - war-time, in, (1943) 340, 343, 348
- Scalds, (1941-2) 178, (1943) 167 *See also* Burns
- Scalenus
 - muscle, procaine hydrochloride injection into, (1941 2) 189
 - cervical rib and, (1940) 245
 - syndrome, (1941-2) 189
- Scalp
 - carcinomatous metastases confined to, (1940) 535
 - ringworm, gentian violet treatment, (1940) 304
 - wounds, treatment of, (1941 2) 196
- Scaphoid, carpal, internal fixation of fractured, (1941-2) 211
- Scar
 - operation, prevention of keloid formation in, (1943) 256
 - post-operative, endometriosis in, (1943) 201
- Scarlet fever, (1939) 525, (1940) 513-5
 - aetiology, transmission by milk, (1943) 328
 - antitoxin, (1940) 514
 - complications, prevention of, (1943) 329
 - diagnosis, (1941 2) 67
 - gangrene of feet complicating, (1941 2) 378
 - immunity and vaccination, (1939) 526
 - immunization,
 - formol-toxoid and tannic acid precipitated toxin, (1943) 329
 - intradermal standard toxin, (1943) 330
 - oral, (1943) 329
 - toxin in tablet form, (1941-2) 378
 - intradermal injection, reaction after, (1943) 330
 - jaundice complicating, (1939) 525
 - liver function test in, (1940) 513
 - nephritis complicating, (1941 2) 313
 - peritonitis, acute haemolytic streptococcal, complicating, (1943) 526
 - post-operative, acriflavine and proflavine in prevention of, (1941-2) 330
 - prognosis, (1940) 513
 - prophylaxis, (1940) 514, (1941 2) 67
 - specific, (1939) 77
 - return cases, (1943) 330

Scarlet fever—continued

- treatment, (1940) 514, (1941-2) 67
 - comparative evaluation, (1943) 329
 - fasting, (1940) 515
 - serum and sulphonamide compounds, comparative value of, (1940) 514
 - sulphanilamide, (1939) 526
 - sulphonamide compounds, (1940) 514
- Schamberg's disease, (1940) 235
- Schaumann's disease, (1943) 347
- Schick test
 - bullous reactions in, (1941-2) 209
 - diphtheria, in, (1940) 272, (1943) 190-2
- Schilder's disease, aetiology, (1940) 515
- Schistosomiasis, stibophen in, (1940) 136
- Schizophrenia, (1941-2) 366, (1944) 347-50
 - aetiology, (1940) 489
 - anti-insulin substance in blood in, (1943) 64
 - brain metabolism in, (1943) 64
 - catatonic pupil in, (1944) 348
 - cerebral circulation in, (1940) 56
 - classification, (1941 2) 366
 - clinical picture, (1940) 489, (1944) 347
 - convulsion therapy, (1939) 116, (1940) 57, 58, 59, 490, 496, (1941 2) 80, (1944) 348-50
 - See also* Psychoses
- ammonium chloride, (1941-2) 368, (1944) 349
- cardiazol,
 - blood pressure during fit, (1940) 492
 - curare for prevention of traumatic complications, (1940) 491
 - insulin premedication, (1940) 493
 - pathological changes, (1940) 490
 - prevention of febrile, (1940) 493
 - status epilepticus as complication, (1940) 493
- death after, (1944) 349
- disturbance of memory, and, (1940) 491
- electrically induced, (1940) 494, (1941-2) 368, (1943) 4, 66, (1944) 349
- faradic, (1941 2) 368
- fractures and dislocations caused by, (1940) 491
- hypoglycaemic, epileptiform seizures complicating, (1940) 494
- insulin, (1940) 58, 493, (1941 2) 367, (1943) 66, (1944) 348
 - compression fractures of spine, (1941 2) 367
 - economical war-time method, (1941 2) 367
 - intravenous administration, (1941-2) 368
- leptazol (cardiazol), (1941-2) 366, 368
- cardiovascular patients, in, (1941 2) 367
- fractures due to, (1941 2) 366
- memory defects after, (1941 2) 367
- results of, (1941-2) 367
- nitrogen gas, (1940) 496
- prevention of traumatic complications in, (1943) 66, 317
- psychology of, (1940) 490
- 'sadistic therapy', (1944) 349
- spinal anaesthesia in, (1944) 349
- triazol, (1941 2) 368
- course and prognosis, (1940) 489
- diabetes mellitus associated with, (1943) 317
- definition and nomenclature, (1941 2) 366
- dys-symbolic, (1940) 489
- electroencephalography in, (1943) 65
- emotional immaturity and regression, (1944) 347
- hippuric acid excretion in, (1940) 489
- liver function tests in, (1940) 55
- nitrogen storage in, (1940) 54
- prognosis, (1940) 58, 489
- Simmonds's syndrome, and, (1940) 530
- thyroxine, administration of, (1940) 54
- treatment, (1940) 490-6, (1941 2) 366, (1944) 348-350
 - glandular extracts, (1940) 495
 - pituitary extract, (1940) 495
 - protamine zinc insulin, (1940) 452
- Schmorl's spondylitis deformans, (1943) 137
- School Medical Service, (1944) 6
- Schuller-Christian syndrome, (1941 2) 287
 - diagnosis, (1943) 266
 - middle ear and temporal bone, involving, (1941-2) 287
- morbid anatomy, (1943) 266

CUMULATIVE INDEX

Schumin's test, (1941-2) 170
 Schwannoma, eyelid, of, (1940) 298
 Schwann's membrane, tumour of, (1940) 298
 Sciatica, (1939) 526, (1943) 4, 210, 330, (1944) 362-366
 aetiology, (1940) 515
 back pain and, (1944) 362-6
 cerebrospinal fluid, changes in, (1939) 526
 diagnosis, (1939) 527
 Forces, in, (1944) 364
 intervertebral disks and, (1943) 331, (1944) 363-366
 dislocation and lesion of, (1940) 516, (1941-2) 14
 lipiodol, use of, (1944) 364
 protruded, as cause of persistent, (1940) 6
 removal of and subsequent bone grafting, (1944) 365
 ligamentum flavum, thickening of, causing, (1940) 515
 morbid anatomy, (1943) 331
 myalgic spots in, (1944) 364
 nucleus pulposus, prolapse of, (1944) 365
 pain, in, review of, (1944) 363
 recent work on, (1944) 365
 soldiers, in, (1944) 364
 treatment,
 lumpectomy, (1944) 364
 procaine, (1944) 364
 sodium salts, intravenous, (1940) 516
 strapping, adhesive, (1939) 527
 surgical, (1944) 365
 X-ray investigation, (1944) 362
 Science, clinical, (1940) 8
 Scleritis necroticans, (1940) 254
 Sclerodactyly, Raynaud's phenomenon associated with, (1941-2) 374
 Scleroderma, (1939) 527, (1940) 527, (1943) 348, (1944) 366
 aetiology, (1940) 516
 dermato-sclerodema of Hardy, (1939) 527
 nerve injury, after, (1940) 516
 oedematous, of Hardy, (1940) 517
 progressive, relation to dermato-myo-sitis, (1941-2) 379
 pulmonary fibrosis in Raynaud's phenomenon, (1941-2) 375
 X-ray therapy, (1940) 517
 Sclerodema adultorum, (1940) 517
 Scleromalacia perforans, (1940) 254
 Sclerosing solutions, diverticula of bladder treated with, (1944) 156
 Sclerosis
 amyotrophic lateral, (1941-2) 307, (1943) 281, (1944) 304
 disseminated, (1940) 6, (1943) 196
 primary lateral, (1944) 304
 tuberos, (1943) 204 *See also* Epiloia
 Scoliosis, (1939) 545
 aetiology, (1940) 539
 empyema, pyogenic non-tuberculous, causing, (1940) 539
 prevention, (1940) 539
 treatment,
 bone traction in, (1940) 539
 conservative methods, by, (1941-2) 396
 Scopulamine, pupil, effect on, (1940) 449
 Scorpion stings, (1939) 241, (1941-2) 161
 toxin of, antidotes to, (1940) 448
 Scott's
 dressing, rheumatism treated with, (1941-2) 229
 wide-field X-ray therapy, (1940) 104
 Scrotum
 diseases, (1941-2) 325
 elephantiasis,
 lymphopathia venereum, in, (1940) 398
 surgical treatment, (1941-2) 325
 haemangioma, (1941-2) 325
 mule-spinner's cancer, (1941-2) 392
 tumours, (1941-2) 325
 Scurvy, (1939) 528, (1941-2) 5
 aged, in, (1941-2) 425
 ascorbic acid concentration and complementary serum activity, (1939) 528
 bones in, (1940) 517

Scurvy—*continued*
 infantile, (1941-2) 379
 physical signs in, (1943) 331
 radiological diagnosis, (1940) 517
 Sebaceous carcinoma, (1943) 345
 Seborrhoea, treatment, liver extract and vitamin B, (1944) 367
 Seborrhoeic dermatitis, treatment, liver extract and vitamin B, (1944) 366
 Seborrheoides, (1944) 366
 Secretin, therapeutic uses of, (1940) 454
 test, diagnosis of pancreatic diseases, in, (1941-2) 322
 Sedation, tetanus, in, (1941-2) 407
 Sedatives, (1940) 135
 barbiturates as, (1941-2) 332
 menopausal symptoms treated with, (1941-2) 191
 oxygen, sedative effect of, (1940) 173
 pre-anaesthetic, (1941-2) 143
 Sedimentation rate
 gynaecology, in, (1939) 34
 malignant disease, in, (1941-2) 163
 prognostic value of, (1944) 159
 pulmonary tuberculosis, in, (1944) 70, 159
 Selenium, poisoning, in endemic areas, (1941-2) 410
 Semen
 examination of, in sterility, (1940) 543
 fertility, relation to, (1940) 543
 Semilunar cartilages, cysts of, (1940) 362
 Seminoma
 abdominal testis, of, (1941-2) 405
 teratoma and, concurrent, (1941-2) 405
 traumatic displacement of testis resulting in, (1941-2) 405
 Senescence and senility, (1939) 528, (1940) 518, (1941-2) 379, (1944) 367 *See also* Old age
 centenarians,
 blood changes, (1939) 529
 cardiovascular system, (1939) 529
 clinical picture, (1939) 528
 observations on, (1939) 528
 dangers of exercise, (1943) 331
 deafness caused by, (1944) 367
 keratoderma, (1941-2) 191
 osteoporosis of spine, (1941-2) 381
 (Redlich-Fischer) plaques, (1943) 113
 toxic exhaustion syndromes, treatment of, (1941-1942) 82
 vaginitis, treatment, (1944) 27
 vitamin treatment in, (1943) 331
 Sensation, physiological unit of, (1943) 74
 Sensibility, cutaneous, (1943) 74
 Sensory innervation of the skin, (1943) 74
 Sepsis
 penicillin, use of, (1944) 326
 puerperal *See* Puerperal sepsis
 Septicaemia and bacteraemia, (1939) 530, (1944) 367-9
 chemotherapy, in (1941-2) 58
 gangrenous meningococcal purpura, treatment, (1939) 530
 gonococcal, (1941-2) 237
 meningococcal, (1941-2) 4
 penicillin, use of, (1944) 326
 staphylococcal,
 bacteriophage in, (1940) 519
 M & B 693 in, (1939) 530
 penicillin in, (1944) 368
 sulphapyridine in, (1940) 519
 sulphathiazole in, (1941-2) 342, (1944) 332
 streptococcal,
 serum and sulphanilamide therapy, (1939) 530
 sulphathiazole in, (1940) 519, (1941-2) 342
 sulphonamides in, (1940) 12
 treatment, sulphonamides, (1941-2) 115
 Septum
 interauricular, defects of, (1941-2) 247
 interventricular, rupture of, due to cardiac infarction, (1941-2) 146
 recto-vaginal endometriosis of, (1941-2) 221
 ventricular, transposition of great vessels with defect of, (1941-2) 248

CUMULATIVE INDEX

Serum

- amylase test, diagnosis of pancreatitis, in, (1943) 296
- pancreatic disease, in, (1944) 20
- cholinesterase determination in biliary disease, (1944) 287
- concentrated, in shock, (1940) 528
- convalescent,
 - infants, vaccination of, effect on, (1940) 579
 - rheumatism, acute, in, (1940) 511
 - human, as blood substitute, (1940) 218
 - interchangeability of plasma and, (1940) 221
- jaundice, (1944) 35
- phosphatase test, (1939) 247
- protein, (1941-2) 305
 - wound healing, relation to, (1941-2) 263, 268
- sickness, treatment of, (1939) 201
- therapy,
 - anthrax, (1941-2) 147
 - antipertussis, (1943) 380
 - cerebrospinal fever, in, (1939) 274, (1940) 245, (1941-2) 187, (1943) 172
 - chemotherapy in pneumonia, and, (1941-2) 354
 - convalescent serum,
 - measles, in, (1941-2) 302
 - poliomyelitis, in, (1941-2) 356
 - diphtheria, in, (1940) 3
 - measles, in, (1944) 300
 - prophylaxis, (1943) 279
 - meningitis, in, (1939) 275, 429
 - multiple neuritis sequel of, (1939) 446
 - pityriasis rosea, (1940) 467
 - pneumococcal meningitis, in, (1940) 404
 - pneumonia, in, (1940) 472, (1941-2) 354, (1943) 310
 - poliomyelitis, in, (1941-2) 356
 - scarlet fever, in, (1940) 514
 - sulphonamide compounds and, (1940) 245, 404, 472
 - tetanus, in, (1940) 3
 - whooping-cough, in, (1940) 595
 - yellow fever, in, (1943) 381
- transfusion,
 - advantages and disadvantages in acute cases, (1943) 157
 - nephrotic syndrome treated by, (1943) 289
 - reactions, (1943) 157
- Sesame oil, substitute for olive oil, (1940) 127
- Sex factor in longevity, (1941-2) 379
- Sex hormones, (1939) 531, (1944) 47, 369 *See also*
 - Androgens. Endocrines, pharmacological aspects. Hormones, sex
 - carcinogenic properties, (1944) 173
 - female, (1944) 369
 - gonadotrophic substances, (1939) 531
 - anterior-pituitary-like hormone, gastric acidity, effect on, (1939) 532
 - spermatogenesis, effect on, (1939) 531
 - immune body, production of, (1939) 531
 - ovulation, production of, (1939) 532
 - peptic ulcer, uses in, (1939) 532
- male, (1939) 534
 - chemistry, general review of, (1944) 369
 - hypogonadism and surgical castration, (1939) 534
 - lactation, suppression of, (1939) 536
 - male breast, hypertrophy of, (1939) 535
 - menopausal disturbances, in, (1939) 536
 - menstrual disturbances, in, (1939) 536
 - prostatic enlargement, in, (1939) 535
 - vascular changes, (1939) 536
- oestrogenic substances, (1939) 532
 - blood of pregnant women, in, estimation of, (1939) 532
 - endometrium, effect on structure of, (1939) 533
 - gastric acidity, effect on, (1939) 533
 - mammary growth, stimulation of, (1939) 533
 - stilboestrol, toxicity of, (1939) 533
 - yohimbine, absence of oestrogenic activity, (1939) 534
- oestrogens *See* Oestrogens
- progestogens *See* Progestogens
- subcutaneous implantation of pellets, (1939) 531
- therapy, (1944) 53
 - abortion, threatened and habitual, (1944) 52
 - amenorrhoea, (1944) 51

Sex hormones--continued

- therapy--continued
 - atrophic rhinitis, (1944) 314
 - bleeding, functional, (1944) 51
 - dysmenorrhoea, (1944) 52
 - eunuchism, (1944) 49
 - eunuchoidism, (1944) 50
 - female, in, (1944) 51
 - impotence, psychogenic, (1944) 50
 - involutional psychoses, (1944) 347
 - lactation, (1944) 52
 - leucoplakia, buccal, (1944) 53
 - male, in, (1944) 49
 - mammary glands, (1944) 52
 - mastopathia, (1944) 52
 - menstrual and climacteric disorders, (1944) 369
 - otosclerosis, (1944) 53
 - prostatic hypertrophy, (1944) 50
 - rhinitis, atrophic, (1944) 53
 - sterility, (1944) 50, 52
- Sexual behaviour and abnormalities, (1940) 527, (1941-2) 385
- Sheep, ecthyma contagiosum, virus disease of, (1941-2) 217
- Shell shock, (1940) 486
- 'Shelter foot', (1943) 2
- Shigella*
 - organisms, ulcerative colitis, in relation to, (1939) 286
 - paradysenteriae* infections, sulphathiazole in, (1943) 188
- Shock, (1941-2) 1, 8, 385, (1944) 370
 - adrenal secretions, role of, (1941-2) 386
 - air-raids, in, (1943) 314
 - anaesthetics, choice of, (1941-2) 388
 - blood pressure in, (1941-2) 1, 40
 - blood studies in, (1940) 528
 - burns, in, (1940) 236, (1941-2) 179
 - cerebral fat embolism and, (1943) 337
 - collapse, and, (1939) 537
 - hypothesis of, (1939) 537
 - post-operative, (1939) 537
 - correlation with multiple coronary occlusions, (1943) 125
 - cortin, pre-operative administration of, (1941-2) 387
 - estimation of degree of, (1941-2) 1
 - experimental, pateridrinol in, (1941-2) 388
 - fat embolism and, (1941-2) 386
 - foetal, desoxycorticosterone acetate in, (1943) 338
 - haematogenic, (1944) 370
 - haemorrhage causing, (1943) 338
 - histamine-like substance, role of, (1941-2) 386
 - hypotheses of, (1941-2) 386, (1944) 370
 - indications for operation in, (1941-2) 9
 - injury and, (1941-2) 386
 - morphine in relation to, (1944) 271
 - muscle extracts, effect on heart, (1944) 370
 - neurogenic hypothesis, (1941-2) 386
 - obstetric, (1943) 18
 - crush syndrome, relation to, (1943) 19
 - plasma transfusion, (1940) 113
 - post-operative,
 - desoxycorticosterone acetate in, (1944) 371
 - primary, (1941-2) 38
 - restoration of blood volume in, (1941-2) 1
 - review of published records on, (1941-2) 39
 - secondary, (1941-2) 38, 387
 - serum: concentrated, in, (1940) 528
 - sub-endocardial haemorrhages in, (1940) 528
 - surgical,
 - heat and cold, effect of, (1941-2) 387
 - treatment of, (1941-2) 387
 - water and electrolyte balance, control of, (1940) 527
- therapy *See* Convulsion therapy
- amyltal as prognostic test, (1944) 74
- mental diseases, in, (1944) 73
- thiamin, effect of, (1943) 338
- toxaemia and, (1944) 370
- traumatic,
 - nervous factor in, (1941-2) 386
 - splenectomy, effect of, (1941-2) 386
 - thrombocytopenia in, (1941-2) 386

CUMULATIVE INDEX

Shock—continued

- treatment of, (1940) 11; (1941-2) 9, 387
- adrenal cortical extract, (1940) 528
- blood substitutes, use of, (1940) 6
- blood transfusion, (1941-2) 38
- plasma, and, (1941-2) 387
- vasoconstrictor, and, (1941-2) 388
- corticosterone, (1940) 529
- cortin, pre-operative administration of, (1941-1942) 387
- desoxycorticosterone acetate, (1944) 371
- eschatin, (1940) 528
- hypertonic saline, (1941-2) 388
- intravenous transfusions, (1941-2) 387
- mental disease, in, (1939) 116
- neo-synephrin, (1940) 528
- oxygen, (1944) 371
- paredrinol, (1940) 529, (1941-2) 388
- plasma and blood transfusion, (1941 2) 387
- pooled concentrated human serum, (1941-2) 388
- postural, (1941-2) 387
- saline and serum, intravenous transfusions, (1941-2) 387
- wound, (1941-2) 39

Short-wave therapy

- asthma, in, (1939) 233
- dental sepsis, in, (1941-2) 202
- eclampsia, in, (1939) 491
- rotating electrode in, (1939) 326
- sinusitis, in, (1940) 144

Shoulder

- bursitis, acute acromial, surgical treatment of, (1940) 300
- myalgia, acute, of, (1944) 305
- pain,
 - myocardial infection, associated with, (1941-2) 249
 - procaine hydrochloride, use of, in, (1941-2) 189
- painful, treatment of, (1944) 232

Sialectasis, (1940) 513

Sialo-angiectasis, (1940) 513

Siccolam, use in skin lesions, (1941-2) 339

Sickness, air, (1941-2) 36

Sideropenic dysphagia, (1941-2) 128

Sigmoidoscopy, periarthritis nodosa, in, (1943) 132

Sigmoido-vesical fistula, carcinomatosis, (1944) 184

Sign, Hamman's, (1944) 302

Silica, tubercle bacillus, influence on, (1940) 530

Silicosis, (1939) 537, (1940) 529, (1941-2) 389

acute, (1941-2) 389

aetiology, (1940) 529, (1941 2) 389, (1944) 372

clinical picture, (1941-2) 389

dentistry, hazard in, (1940) 529

diagnosis, (1939) 537

heart disease, secondary, in, (1939) 537

miners of bituminous coal, in, (1941-2) 389

morbid anatomy, (1941-2) 389

prevention, (1939) 537

radiological and histological appearances, (1943) 338

sand-blast, rapid onset in, (1941-2) 389

tubercle bacillus, influence of silica on, (1940) 530

tuberculo-, X-ray findings, (1941-2) 390

tuberculosis in relation to, (1944) 372

Silk

suture in infected wounds, (1941 2) 266

suture material, as, (1944) 18

Silver

colloidal, and mercury ointment, in venereal prophylaxis, (1940) 450

ferrihaemoglobin, ophthalmic and otorhino-

laryngological conditions, (1941-2) 339

nitrate, burns treated with, (1941-2) 181

picrate,

suppositories, in vulvovaginitis, (1940) 320

vaginitis treated with, (1943) 379

Simmonds's syndrome, (1939) 538; (1944) 45

aetiology, (1940) 530

anorexia nervosa resembling, (1939) 219

dementia praecox, association with, (1940) 530

diagnostic tests, (1943) 339

differential diagnosis, anorexia nervosa, (1943) 340

hypophyseal necrosis and, (1940) 465

mental and pathological changes, (1943) 339

Simmonds's syndrome—continued

- morbid anatomy, (1940) 530
- necropsy findings, (1943) 339
- pituitary, atrophy of, following tuberculosis, (1940) 531
- post-partum necrosis of anterior pituitary and, (1940) 530
- spontaneous hypoglycaemia in, (1941-2) 92, 390
- Sinine, malaria treated by, (1943) 83, 277

Sinus

- carotid, (1941-2) 2
- dermal, intraspinal, (1943) 349
- frontal,
 - absence or imperfect development of, (1943) 103
 - infection, spreading, (1941-2) 127
- lateral venous, congenital absence of, (1941-2) 216
- maxillary, lipiodol radiography, (1941-2) 127
- median mental, (1940) 412
- nasal accessory, (1940) 144, (1941 2) 127
- lipiodol radiography, (1941-2) 127
- superior longitudinal, thrombosis, (1940) 67
- thrombophlebitis, heparin and sulphonamide therapy, (1941-2) 408
- thrombosis, (1940) 66
- cavernous, (1943) 14
- penicillin in treatment, (1944) 13

Sinusitis

- acute,
 - frontal, infection after, (1941-2) 127
 - sulphathiazole microcrystals in treatment, (1944) 121
 - X-ray therapy, (1941-2) 127
- bronchiectasis, relation to, (1941 2) 127, (1943) 165

chronic,

sodium salt of sulphathiazole in, (1941-2) 127

X-ray therapy, (1941 2) 127

chronic hyperplastic, bacteriology, (1940) 144

paranasal, common cold and, (1944) 180

treatment,

short-wave therapy, (1940) 144

sodium salt of sulphathiazole, (1941-2) 127

X-ray, (1940) 145, (1941-2) 127

Sjogren's disease, (1939) 595, (1940) 263

Skeleton

leukaemia, in, (1941-2) 286

X-ray examination, (1941-2) 371

Skin

- abnormalities, (1941-2) 230
- action of various drugs on, (1941-2) 331
- allergy of, (1941-2), (1943) 112
- colour and cancer, (1941-2) 394
- cutaneous horns, (1943) 345
- eruptions,
 - sulphapyridine causing, (1941-2) 213
 - sulphonamides causing, (1941-2) 344
- gangrene, progressive, (1941-2) 392
- grafting, (1941-2) 264
- burns, in treatment of, (1939) 269
- ulceration of leg, in, (1944) 395
- leptosy, in, (1940) 380
- lesions,
 - adenopathy, giant follicular, and, (1943) 275
 - lymphosarcoma, (1943) 274
 - malformations of, and heredity, (1943) 344
- pigmentation, ultra-violet irradiation and blood transfusion producing, (1940) 151
- pre-operative preparation of, (1941-2) 331
- reactions during sulphathiazole therapy, (1940) 460
- sensory innervation of, (1943) 74
- systemic conditions, (1941 2) 395
- vitamin A deficiency, in, (1940) 271
- Skin diseases, (1941-2) 390, (1944) 372-5
- amoebiasis of, (1941-2) 138
- amyloidosis, localized, of, (1943) 115
- avitaminosis and, (1943) 377
- cancer, mule-spinner's, (1941-2) 392
- dermatosis. *See also* Dermatitis
- Grenz ray treatment, (1943) 323
- Ehlers-Danlos disease, (1940) 301
- fat metabolism in, (1944) 375
- Fox-Fordyce disease, (1944) 374
- Hodgkin's disease, (1944) 251

CUMULATIVE INDEX

- Skin diseases—continued**
infections, locally inoculated, (1940) 532, (1941–2) 392
insects and acarines causing, (1940) 531
leucoplakia, (1941–2) 394
lice causing, (1940) 531
necrobiosis lipoidica diabetorum, (1941–2) 395
necrosis, spreading, (1941 2) 392
occupational, (1941–2) 392, (1944) 373
 collier's stripes, (1940) 259
 fur industry, (1944) 260
 prevention, (1940) 260
parasitic, (1943) 340, 348
 treatment, (1943) 348
 war and, (1943) 340, 343, 348
phrynodermia, (1939) 538
 vitamin A treatment, (1939) 538
pyogenic,
 sulphanilamide in, (1940) 260
 sulphonamide ointment in, (1944) 199
treatment, (1941–2) 120
 siccolam, use of, (1941–2) 339
 sulphapyridine in experimental pneumonia, (1941 2) 342
tuberculosis, (1939) 64, 538
 rubrophen in treatment, (1939) 538
 vitamin A and, (1930) 128
 vitamin C and, (1940) 588
X-ray therapy, (1941–2) 373
 dosage in, (1940) 504
- Skin tumours,** (1939) 539, (1940) 533–5, (1941 2) 393, (1943) 344, (1944) 373
benign, (1940) 533
 calcinosis, sodium citrate and calcium gluconate in treatment, (1939) 539
 carcinoma, (1940) 534, (1943) 344–6
 acrodermatitis chronica atrophans, in, (1943) 346
 bronchogenic carcinoma, secondary to, (1940) 394
 Kaposi's pigmentary sarcoma, (1943) 347
 melanotic,
 incidence in coloured races, (1940) 534
 radio-sensitivity, (1939) 541
 metastatic, confined to scalp, (1940) 535
 prognosis, (1940) 241, 534
 rodent ulcer, (1943) 345
 skin colour, significance of, (1941 2) 394
 squamous-celled, radium therapy, (1939) 540
 X-ray treatment, (1941 2) 394, (1944) 374
- dermatofibroma,** (1941 2) 393
fibrous tissue, derived from, (1941–2) 393
glomangioma, (1940) 533
glomus, (1941–2) 393, (1943) 345
hair follicles, derived from, (1941–2) 393
innocent, (1941–2) 393, (1944) 373
infective, (1940) 533, (1941 2) 394, (1943) 347
keratoses, (1941–2) 394
lymphocytoma, military, (1939) 540
malignant, (1940) 534, (1941 2) 394, (1944) 374
naevi, thorium-X in treatment, (1939) 539
X-ray treatment, (1944) 374
nerve tissue, derived from, (1940) 533, (1941 2) 393
precanceroses, (1941–2) 394
sarcoïd, (1943) 347
 Boeck's, (1939) 541, (1940) 533, (1941–2) 394
 clinical picture, (1944) 375
 sarcoma, Kaposi's pigmentary, (1944) 374
 superficial layers, derived from, (1941–2) 393
 sweat glands, derived from, (1944) 374
 trichoeptithelioma, (1939) 539
warts, plantar, X-irradiation of, (1939) 539
xanthoma, (1940) 534
- Skull**
craniofacial, (1944) 233
fenestrae parietales symmetricae, (1940) 224
fractures,
 ear involvement, (1940) 49–53
 posterior pituitary, injury to, and, (1941 2) 174
 recurrent pneumococcal meningitis after, (1940) 404
- Sleep**
disorders, (1941–2) 85
paralysis, (1943) 287
recorders, (1941–2) 85
Sleeping sickness *See* Trypanosomiasis
Smallpox
 Asiatic, (1944) 376
 epidemiology, (1944) 61
 Glasgow outbreak, (1944) 376
 herpes zoster, association with, (1943) 242
 incidence, (1944) 376
 recent work on, (1944) 61
Smith-Petersen nail, fractures of hip treated with, (1944) 20
Smoke, dermatitis caused by, (1944) 198
Smokers, hypnosis treatment in, (1939) 378
 blood pressure, effect on, (1939) 249
Smoking
 coronary disease and, (1941 2) 152
 gastric acidity, effect on, (1941–2) 326
 peptic ulcer, accessory cause of, (1940) 26
 peripheral
 vascular system, effect on, (1940) 196
 vasospasm resulting from, (1940) 557
 thrombo-angitis obliterans and, (1941–2) 151
- Snake**
bite and antivenenes, (1939) 242
venom,
 application in various diseases, (1943) 303
 herpes simplex treated with, (1941 2) 256
- Snuff**
antiseptic, for nasal infections, (1941–2) 331, (1943) 100, 305
sulphathiazole, (1943) 171
Soap, containing sulphur, scabies treated with, (1943) 343
Soap-lather, ocular infections treated with, (1940) 445
Sobismolnol mass, syphilis treated with, (1940) 548
Social factors in relation to mortality, (1939) 280
Sodium
acid sulphate, poisoning by, (1941–2) 408
amylal,
 benzedrine and paredrine, interruption of anaesthesia by, (1940) 178
 convulsion therapy, use in, (1941 2) 79
 mental diseases, prognosis and in, (1940) 59
 psychotherapy, use in, (1944) 344
ascorbate, intravenous injections of, in haemorrhage, (1941 2) 269
bicarbonate,
 scorpion stings, treatment of, in, (1941–2) 161
 vitamin C in treatment of erythraemia, and, (1941 2) 225
bis(*p*-aminophenyl)-sulphone-dextrose sulphonate (promander), (1943) 62
bismuth thioglycollate, malaria therapy, use in, (1940) 400
chloride *See also* Salt
 bromide eruptions treated with, (1941–2) 213
 deficiency, (1940) 113
 pneumonia treated with cortin and, (1941 2) 355
citrate,
 lead poisoning treated with, (1944) 284
 compounds of sulphonamides, (1941–2) 340, 346
diphenylhydantoinate, (1941 2) 113, (1943) 95
anticonvulsant properties, (1940) 454
 compared with other anticonvulsant drugs, (1941–2) 222
epilepsy, in, (1939) 126, (1940) 135, 291–3; (1941 2) 222, (1944) 230
hemiplegia after treatment with, (1940) 293
infantile convulsions treated with, (1941–2) 197
large doses, effect of, (1941–2) 339
toxic effects, (1940) 454
 mentally defective, in, (1941–2) 223
fluoride, poisoning by, (1944) 386
formaldehyde sulphonylate, mercury poisoning treated with, (1940) 555
free diet, Ménière's syndrome treated by, (1943) 377
hypochlorite, treatment of burns, in, (1941–2) 114
iodide, scatica treated by intravenous injection of, (1940) 516

CUMULATIVE INDEX

Sodium—continued

lactate, intravenous dextrorotary, use in liver function test, (1944) 287
metabolism, (1940) 113
morrhuate, (1941-2) 112
bursitis, radio-humeral, treated with, (1940) 300
chronic obstructive rhinitis, injections in, (1941-1942) 317
oesophageal varices, injection in, (1940) 428
sensitivity to, (1941-2) 421
varicose veins, for, reactions after, (1940) 581
psylliate, chronic obstructive rhinitis, submucosal injections of, in, (1941-2) 317
recinoleate, methylene blue and, in otosclerosis, (1940) 255
varicose veins treated with, (1944) 399
salicylate,
absorption and excretion after rectal administration, (1941-2) 339
sciatica treated by intravenous injection of, (1940) 516
succinylmethylamide-*p*-arsonate. *See* Neocryl sulphacetamide, (1943) 99
sulphamethylthiazole, urinary tract complications due to, (1941-2) 346
sulphapyridine,
cerebral symptoms arising from, (1941-2) 187
cerebrospinal fever, in, (1941-2) 187
intravenous administration of, (1940) 471
lobar pneumonia, in, (1941-2) 354
urinary tract complications due to, (1941-2) 346
sulphate, hypertonic,
and acriflavine, in infected wounds, (1941-2) 268
wound dressing, as, (1940) 351
sulphathiazole,
common cold treated with, (1944) 181
urinary tract complications due to, (1941-2) 346
tetrathionate, thrombo-angitis obliterans treated with, (1940) 194
thioethamyl, basal narcotic, as, (1939) 211
thiosulphate,
excretion of arsenic, effect on, (1941-2) 404
thrombo-angitis obliterans treated with, (1940) 194
thorium tartrate, use in radiography, (1941-2) 371
Soft-tissue radiography, (1940) 102
pregnancy, in, (1941-2) 280
Solantoin, (1941-2) 113, (1943) 95
epilepsy treated with, (1940) 135
Soldiers. *See also* Forces, War
abdominal emergencies in, (1943) 11
body armour for, (1940) 11
bronchiectasis in, (1944) 68
cardiovascular diseases in, (1941-2) 44
depressive states in, (1943) 316
digestive
diseases in, (1944) 214
disorders in, (1940) 25, (1943) 2, 198
dyspepsia in, (1941-2) 4, 214
effort syndrome in, (1941-2) 244, 245
foot,
disease in, (1941-2) 232
pain in, (1944) 236
fractures in, (1943) 12
group intelligence tests in, (1944) 78
heart disease in, (1940) 329-31; (1941-2) 2, 244, (1943) 231 *See also* Effort syndrome
hernia in, (1943) 10
impetigo in, (1944) 257
intestinal obstruction in, (1943) 12
malignant disease in, (1943) 12
mass radiography in, (1943) 319
night-blindness in, (1943) 206
nutrition of, (1940) 11
paralysis, hysterical, in, (1941-2) 363
psychoneuroses in, (1940) 61
rheumatism in, (1943) 209
sciatica in, (1944) 364
tuberculosis, pulmonary, in, (1944) 290
Soleus muscle, lipoma in, (1941-2) 310
Soluble
dilantin, (1941-2) 113
phenytoin, (1941-2) 113
rod method of vascular anastomosis, (1941-2) 264

E.M.S. II

Soluseptasine, (1940) 133
chemistry and pharmacology of, (1939) 170
Corynebacterium diphtheriae, action on, (1941-2) 341
Solustibosan, kala-azar, in, (1939) 148
Solvents, volatile, toxicology of, (1944) 387
Somnolence, periodic, and morbid hunger, (1943) 318
Soneryl poisoning, picrotoxin in, (1940) 558
Sorbitol
dehydrating agent, as, (1941-2) 339
glaucoma, in, (1939) 350
Spasm, treatment of, (1939) 165
Spasmophibia, vitamin D and, (1940) 130
Specific fevers, infant mortality, in relation to, (1939) 41
Spectacles, eye injuries from broken, (1940) 253
Speech defects, (1939) 542; (1940) 535; (1944) 376
aetiology, (1944) 377
hearing defects, relation to, (1940) 535
treatment,
hypnosis in, (1940) 536
psychological, (1939) 543
stuttering, (1939) 542
Spermatic cord,
inguinal hernia, in, transplantation, (1941-2) 255
torsion, (1943) 360
Spermatogenesis, sulphanilamide, effect of, (1940) 543
Spermatozoa
sterility, relation to, (1940) 543, (1944) 379
survival of, effect of pus on, (1941-2) 399
Spermicidal preparations, (1941-2) 197
Sphincter ani, surgical repair of, (1944) 359
Sphygmomanometers, (1943) 149
Spina bilida, meningocele associated with cranio-lacunaria, (1941-2) 396
Spinal
anaesthesia. *See also* Anaesthesia
nupercaine, (1944) 136
pulmonary tuberculosis, in, (1944) 136
appendicitis, (1941-2) 125
canal, myeloscope in examination of, (1940) 67
cord,
blood supply of, (1939) 120
diseases, (1939) 543, (1941-2) 395
arachnoiditis, chronic adhesive, (1939) 544
compression by hernia of nucleus pulposus, (1939) 543
dermal sinuses, (1943) 349
familial neuromyelitis optica, (1939) 544
ischaemia, in dissecting aortic aneurysm, (1943) 123
subacute combined degeneration, (1939) 543, (1941-2) 396
ankylostomiasis and, (1940) 187
injections into, headache, and, (1940) 110
radiography, (1941-2) 371
tumours, (1943) 349
dermoid, (1943) 349
epidermoid, (1943) 349
extrathecal, (1944) 377
lymphoblastoma, (1944) 377
melanoma, primary, of, (1940) 536
vascular anomalies, (1943) 349
osteoporotic type of hyperparathyroidism, (1941-1942) 322
Spine
anaesthetic procedures around, (1944) 85
clay-shoveller's fracture, (1940) 276
diseases and deformities, (1939) 544; (1940) 536-540; (1941-2) 396
Calvé's, (1940) 539
epidural abscess, (1941-2) 397
epiphysitis, (1940) 296
inflammatory, (1941-2) 397
fractures, (1940) 276
insulin shock therapy causing, (1941-2) 367
leptazol shock therapy causing, (1941-2) 366
-fusion operation for spinal tuberculosis, (1941-1942) 396
hyperparathyroidism, in, (1941-2) 322
intervertebral disk. *See* Intervertebral disk
prolapse of, (1939) 545

2 L

CUMULATIVE INDEX

Spine—continued

- intervertebral disk—continued
 - protruded, (1941–2) 396
 - ruptured, (1943) 350
 - irradiation of, in herpes zoster, (1941–2) 256
 - osteoarthritis, (1943) 137
 - physiotherapy, (1944) 154
 - osteomalacia, (1939) 546
 - osteomyelitis, acute, treatment, (1941–2) 397
 - osteoporosis, senile, (1941–2) 381
 - Pott's disease. *See* Tuberculosis
 - scoliosis, (1939) 545
 - conservative methods in, (1941–2) 396
 - specific bone diseases, manifestation of, (1941–2) 396
 - spondylolisthesis, (1939) 545; (1940) 540
 - tuberculosis, (1939) 544
 - paraplegia, surgical treatment of, (1939) 544 (Pott's disease),
 - multiple pathological fractures in, (1940) 536
 - spine-fusion operation, (1941–2) 396
 - surgery, (1939) 544
 - undulant fever, lesions in, (1940) 573
- Spiritus vini rectificatus, herpes labialis treated with, (1941–2) 256
- Spirochaeta*
- pallida*, (1940) 87
 - cultivation of, (1943) 87
 - survival in frozen plasma, (1944) 102
 - recurrentis*, (1943) 325
- Spirochaetes, presence in gastric mucosa, (1941–2) 401
- Spirochaetosis icterohaemorrhagica, (1940) 358
- nervous complications, (1940) 358
 - occupational hazard, as, (1943) 255
 - serological test, rapid presumptive, (1940) 358
- Splanchnectomy, supradiaphragmatic, in essential hypertension, (1941–2) 164
- Spleen
- agnogenic myeloid metaplasia of, (1940) 541, (1943) 351
 - Banti's syndrome, (1941–2) 398, (1943) 351
 - diseases, (1939) 546, (1940) 541, (1941–2) 397
 - accessory spleens, (1939) 546
 - aneurysm, rupture during pregnancy, (1944) 25
 - Gaucher's disease, lipid analysis of, in, (1943) 265
 - enlargement, (1941–2) 397. *See also* Splenomegaly
 - hepato-lenal fibrosis, (1941–2) 398
 - infarct, septic, (1940) 541
 - leukaemia, in, (1944) 285
 - primary portal phlebosclerosis in children, (1943) 351
 - reticulo-endotheliosis, (1939) 547
 - tuberculosis, (1940) 541
 - vascular changes associated with, (1941–2) 397
 - Werlhof's disease (purpura haemorrhagica), (1939) 547
 - X-ray therapy in, (1940) 6
 - excision, effects of, (1943) 350
 - post-traumatic splenic implants, (1943) 351
 - rupture of, (1943) 351
 - glandular fever, in, (1941–2) 235
- Splenectomy
- acholuric jaundice, in, (1939) 207
 - anaemia, in, (1939) 55
 - achrestic, (1939) 204
 - Banti's syndrome, in, (1941–2) 398
 - effects of, (1943) 350
 - essential thrombocytopenia treated by, (1941–2) 241
 - rheumatoid arthritis, in, (1940) 199
 - traumatic shock, effect in, (1941–2) 386
- Splenic
- artery, aneurysm of, (1941–2) 398
 - implants, post-traumatic, (1943) 351
 - puncture, kala-azar, in, (1940) 362
- Splenomegaly lymphatica hyperplastica, (1940) 343
- Splenomegaly
- Ascoli's treatment, (1941–2) 398
 - chronic, (1943) 351
 - malaria causing, (1940) 541

Splenomegaly—continued

- leukaemia, in, (1944) 285
 - tuberculosis, (1940) 541
 - vascular changes associated with, (1941–2) 397
- Splint
- rheumatoid arthritis, in, (1941–2) 154
 - vitalium, use of, (1941–2) 210
- Spondylarthritis ankylopoietica, (1941–2) 155
- Spondylitis
- adolescents, X-ray therapy, in, (1940) 105
 - ankylosing, (1941–2) 155
 - deformans, endocrine therapy, (1940) 200
- Spondylolisthesis, (1939) 545
- aetiology of, (1940) 540
 - fourth lumbar vertebra, of, (1941–2) 161
- Spondylosis deformans, Schmorl's, (1943) 137
- Spore-forming bacteria, milk, in, (1941–2) 232
- Sport. *See* Athletics
- Spotted bones, (1941–2) 171
- Sprains, procaine in, (1939) 235, (1941–2) 159
- Spray
- intranasal vaccine, in prevention of colds, (1941–2) 193
 - nasal, (1939) 184
 - danger of, (1939) 285
- Sprue, (1941–2) 26, 398
- aetiology, (1941–2) 398
 - biochemical considerations, (1944) 378
 - differential diagnosis, pernicious anaemia, (1944) 378
 - endocrine disturbances in, (1940) 542
 - fat absorption, mechanics of, (1941–2) 26
 - lacteal obstruction and, (1941–2) 28
 - liver extract in, (1939) 149
 - morbid anatomy and pathology, (1941–2) 27, (1944) 378
 - neutral red excretion test in, (1944) 378
 - nicotinic acid in, (1940) 542, (1941–2) 399
 - non-tropical, (1941–2) 26. *See also* Coeliac disease
 - paralysis of muscularis mucosae, (1941–2) 27
 - pathogenesis of, (1941–2) 26
 - steatorrhoea in, (1944) 378
 - stools in, (1941–2) 26
 - valvular conviventes in, (1941–2) 27
- Sputum
- lobar pneumonia, in, (1941–2) 352
 - pulmonary tuberculosis, in, (1940) 391, (1941–2) 292
 - serial inoculation with, for diagnosis of tuberculosis, (1944) 393
- Staining, supravital, of leucocytes, (1941–2) 7
- Stammering
- aetiology, (1944) 377
 - extraction of teeth for, (1944) 376
 - psychotherapy and re-education, (1944) 377
 - treatment, (1944) 376
- Staphylococcus
- antitoxin, value of, (1939) 17
 - bacteraemia and septicaemia, treatment by sulphathiazole, (1943) 332
 - conjunctivitis due to, (1939) 290
 - germicides, effect on, (1939) 385
 - infection,
 - glucose tolerance and, (1941–2) 306
 - M & B 693 in, (1939) 171
 - neoarsphenamine in, (1941–2) 342
 - penicillin in treatment, (1944) 368
 - quinocaine in, (1941–2) 339
 - renal cortex and, (1940) 364
 - septicaemia, treatment, (1940) 519
 - sulphathiazole in, (1940) 3, 134
 - sulphonamides in, (1939) 171, (1940) 2, 134, 461; (1941–2) 342
 - toxoid, prostatitis treated with, (1941–2) 359
- Staphylococcus*
- albus*, endocarditis, subacute bacterial caused by, (1943) 237
 - aureus*,
 - dermatitis gangrenosa infantum, in, (1939) 300
 - infections, sulphathiazole and sulphamethylthiazole in, (1940) 461
 - sulphonamides in, (1941–2) 342
 - penicillin, effect of, (1944) 325
 - renal cortex infected by, (1940) 364

CUMULATIVE INDEX

Staphylococcus—continued *aureus—continued*

- ultra-violet irradiation of, (1939) 187
- wounds infected by, (1941-2) 267
- pyogenes*, in pemphigus neonatorum, (1941-2) 325
- State and national health, (1939) 3
- medical practitioner in relation to, (1939) 10
- mortality rate, improvement in, (1939) 6, 9
- preventive medicine, (1939) 4, 7
- Public Health Acts, (1939) 6
- Status
 - asthmaticus, fatality during, (1941-2) 158
 - epilepticus, complicating cardiac therapy in schizophrenia, (1940) 493
 - thymico-lymphaticus, aortic diameter in, (1944) 383
- Staub-Traugott effect, (1940) 152
- Steatorrhoea
 - causes and treatment, (1944) 378
 - Giardia lamblia* infestation associated with, (1944) 203
 - hypovitaminosis of fat-soluble vitamins in, (1941-1942) 192
 - idiopathic, (1941-2) 26
 - haemorrhagic diathesis associated with, (1941-1942) 192
 - vitamin K deficiency in, (1941-2) 192
- Stenosis, pyloric. *See* Pyloric stenosis
- Stereoscopic vision in relation to landing of aircraft, (1941-2) 31
- Sterility, (1939) 548, (1941-2) 21, 399, (1944) 378-80
 - absence of ovulation, (1944) 26
 - anovular menstruation, (1944) 26
 - artificial insemination, (1939) 548
 - contributory factors, analysis of, (1943) 352
 - curettag, (1939) 548
 - female,
 - effect of pus on survival of spermatozoa, (1941-1942) 399
 - electrical determination of ovulation, (1944) 379
 - follicular hormone therapy, (1940) 298
 - hormone therapy, (1944) 52
 - lipiodol injection in, (1940) 299
 - pregnandiol, excretion of, (1939) 548
 - recent advances, (1944) 379
 - safe and fertile periods, (1939) 548, (1944) 379
 - stilboestrol, in, (1940) 132
 - treatment, (1944) 379
 - tubal insufflation, by, (1940) 544, (1941-2) 399
 - tubal resection and implantation, (1939) 548
 - investigation and treatment, (1944) 379
 - male,
 - gonadotrophic hormones in, (1940) 543
 - hormone therapy, (1944) 50
 - seminal findings and fertility, (1940) 543
 - sperm examination, (1940) 543
 - spermatogenesis, sulphanilamide and, (1940) 543
 - testicular biopsy in, (1939) 157, (1941-2) 399, (1943) 352, (1944) 380
 - testicular function, diathermy and, (1940) 543
 - treatment, pregnant mare's serum, (1941-2) 400
- Sterilization, (1939) 549
 - female, of, operative methods, (1939) 549
 - injection, solutions intended for, (1941-2) 113
 - male, of, (1939) 158
 - puerperium, in, (1941-2) 22
 - tubal, (1940) 23
 - reopening of tubes sterilized by ligation, (1940) 23
 - ultra-violet irradiation, by, (1940) 150
- Sternal puncture, (1941-2) 6
 - bone marrow function and, (1940) 6
 - Gaucher's disease, in, (1941-2) 287
 - kala-azar, in, (1940) 362
 - leukaemia,
 - diagnosis of, in, (1940) 32
 - lymphocytic, in, (1940) 383
 - malignant disease, diagnosis of, (1940) 569
 - results in disease of, (1939) 247
 - value of, (1939) 21, 52, 206
- Sternal trephine, leukaemia, diagnosis of, in, (1940) 32
- Sternomastoid muscle, ossification of, (1940) 413
- Sternum, suprasternal bones, (1941-2) 371

Subophen. *See also* Fouadin

- pharmacology of, (1940) 136
- Stilbamidine, kala-azar treated with, (1944) 98
- Stilboestrol, (1939) 35, 110, (1943) 97
 - administration of, (1940) 522
 - amenorrhoea, in, (1940) 522
 - carcinogenic action of, (1941-2) 183
 - carcinoma of prostate treated with, (1944) 93
 - climacteric, in, (1940) 248, 522
 - clinical use of, (1940) 20, 131, 522
 - cream, in treatment of pruritus vulvae, (1941-2) 430
 - dipalmitate, therapeutic efficiency of, (1944) 369
 - dipropionate, (1940) 132
 - therapeutic efficiency of, (1944) 369
 - dosage, (1940) 131
 - early pregnancy, in, (1941-2) 383
 - gynaecomastia in male caused by, (1941-2) 383
 - hepatotoxic effect, alleged, (1941-2) 383
 - inhibition of lactation by, (1941-2) 262
 - lactation, effect on, (1940) 132
 - mastodynia treated with, (1940) 132
 - menopausal symptoms treated with, (1941-2) 191
 - menstrual disorders, in, (1940) 131, 248, 522
 - nausea and vomiting, prevention of, during treatment with, (1944) 26
 - physiological properties of, (1940) 20
 - post-partum uterus, effect on, (1941-2) 370
 - progesterone as adjuvant to, (1940) 132
 - pruritus vulvae treated with, (1940) 132
 - sterility treated with, (1940) 132
 - therapeutic efficiency of, (1944) 369
 - toxic effects of, (1939) 533, (1940) 20, 131, 521
 - tumourigenic effect, (1940) 521
 - uterine contractions, effect on, (1940) 372
 - uterine haemorrhage, functional, treated with, (1944) 26
 - vaginitis treated with, (1940) 132
- Still-birth
 - antenatal care in relation to, (1939) 37
 - dietetic deficiency causing, (1944) 22
 - osteochondritis in, (1943) 356
- Still's disease, aetiology of, (1939) 230
- Sting
 - hypersensitiveness to, (1940) 160
 - scorpion, (1941-2) 161
 - wasp, death caused by, (1943) 144
- Stokes-Adams syndrome
 - electrocardiogram in, (1941-2) 246
 - heart block and, (1941-2) 246
- Stomach
 - acidity, (1943) 245
 - blood supply, experimental deprivation of, (1944) 150
 - cancer, animals, in, nematode causing, (1940) 240
 - carcinoma,
 - benign ulcer, differential diagnosis from, (1940) 545
 - depressant effect of carcinoma extracts on gastric secretion, (1941-2) 401
 - dual (kiss) carcinoma, (1941-2) 400
 - edentulous patients, in, (1944) 31
 - gastroctomy, total, for, (1940) 545
 - gastric secretory depressant principle, (1940) 544
 - pernicious anaemia and, (1944) 130
 - radiological diagnosis, early, (1940) 544
 - spirochaetes in gastric mucosa, presence of, (1941-2) 401
 - termination by Lederer's acute haemolytic anaemia, (1941-2) 401
 - total gastrectomy and partial oesophagectomy for, (1941-2) 401
 - total gastrectomy technique, (1941-2) 401
 - cardiac end, diverticula of, (1941-2) 402
 - Castle's factor in pernicious anaemia, (1943) 3, 47
 - changes, following injury to posterior pituitary, (1941-2) 174
 - cholinergic action of morphine on, (1944) 323
 - devascularization, experimental, (1944) 150
 - dilatation, acute, (1939) 550
 - diospyrobezoar, (1940) 546
 - diseases, phenolphthalein test, (1940) 544
 - diverticula of, (1943) 354
 - emotions, effect of, on, (1944) 30

CUMULATIVE INDEX

Stomach—continued

- examination, radiology and gastroscopy, comparative values of, (1943) 202
- foreign bodies in, (1940) 546, (1943) 353
- haemorrhage, uraemia after, (1943) 372
- Hodgkin's disease of, (1940) 343
- infections, mycotic, (1939) 551
- leiomyoma, (1939) 550
- morphine, action of, (1944) 323
- mucosa, heterotopic, (1940) 279
- neurilemmoma, (1943) 353
- phytobezoar, (1943) 353
- polypi, (1944) 380
- polyposis, (1943) 352
- sarcoma, primary, (1943) 353
- surgery of, (1941-2) 14
- syphilis of, (1941-2) 234
- tobacco smoking, effects on, (1939) 551
- tuberculosis,
 - anaemia, pernicious, associated with, (1940) 169
 - lavage in, (1940) 389
 - ulcers, (1941-2) 401
- tumours, (1939) 549; (1940) 544
 - malignant, (1941-2) 400, (1944) 380
 - operative results and prognosis, (1943) 353
 - surgical treatment of, (1939) 549
- ulcer. *See* Gastric and duodenal ulcer; Peptic ulcer

Stomatitis, treatment by chromium trioxide, (1941-1942) 307

Stools *See also* Faeces

- sprue, in, (1941-2) 26
- Stovarsol, dysentery, amoebic, treated by, (1940) 136
- Strabismus, (1939) 551, (1941-2) 402
 - alternating, (1944) 381
 - children, in, (1941-2) 402
 - comitant, (1941-2) 402
 - operative results, (1944) 381
 - treatment, orthoptic technique, (1944) 381
- convergent, operative results, (1944) 381
- diplopia following Caldwell-Luc operation, (1939) 551
- lacquered lenses, advantages and disadvantages of, (1941-2) 402
- latent, (1940) 546
- non-paralytic, (1941-2) 402
- orthoptic treatment of, (1939) 131

Stratigraphy, (1940) 101

Streptococcus

- children, respiratory infections and rheumatic fever in, (1941-2) 377
- conjunctivitis, pseudomembranous, due to, (1940) 252
- cross-infections, (1943) 248
- dermatitis, sulphanilamide in, (1940) 532
- germicides, effect on, (1939) 385
- haemolytic,
 - Dick test, (1941-2) 261
 - glomerulo-nephritis, acute, causing, (1939) 444
 - pantothenate, influence of, (1944) 368
 - pantoyltaurine, influence of, (1944) 368
 - puerperal sepsis, in, (1940) 499
 - rheumatic fever, acute, in, (1940) 511
 - rheumatism, acute, recovery in cardiac lesions of, (1941-2) 377
 - rheumatism, as cause of, (1939) 137
- sulphonamides, in, (1939) 170, (1940) 133, 284
- tonsils, in, (1940) 553
- wound infection, sources of, (1940) 347
- infection,
 - Dick test, reliability of, (1941-2) 261
 - promin in, (1941-2) 336
 - sulphonamides in, (1940) 3, 12, 133, 284, 532
- lupus erythematosus due to, (1940) 396
- mycosis fungoides, in, (1940) 417
- septicaemia, sulphonamides in, (1940) 12, 519
- ulcers, chronic undermining, caused by, (1940) 571
- wounds infected by, (1941-2) 267

Streptococcus

- faecalis*, bactericidal action of sulphonamides, (1943) 307
- pyocyanea*, wounds infected by, (1941-2) 267
- pyogenes*,
 - transmission by milk, (1943) 328
 - wounds infected by, (1941-2) 268

Streptococcus—continued

- viridans*,
 - infection,
 - bacterial endocarditis, treatment, (1941-2) 251
 - diamino-diphenyl sulphone, and, (1940) 134
 - patent ductus arteriosus, ligature of, (1944) 368
 - recovery, with, (1941-2) 250
 - meningitis caused by, (1941-2) 304
 - sulphanilamides, action on, (1940) 133
 - Stromal tumours of choroid plexus, (1941-2) 175
 - Strophanthin
 - electrocardiogram changes due to, (1941-2) 340
 - heart disease, in, (1940) 135, 455
 - Stupor, hysterical, treatment by cardiazol, (1944) 341
 - Sturge's disease, (1939) 551
 - Stuttering, (1944) 376
 - Subacromial bursitis, (1941-2) 189
 - Subacute combined degeneration of spinal cord, (1939) 543. *See also* Spinal cord
 - Subarachnoid haemorrhage. *See* Haemorrhage
 - Subarachnoid injection
 - alcohol, of, for relief of intractable pain, (1941-2) 185
 - procaine, of, (1944) 327
 - Subclavian veins, thrombosis of, (1941-2) 420
 - Subdeltoid bursitis, (1941-2) 189
 - Subendocardial haemorrhages, shock, in, (1940) 528
 - Submaxillary gland, tumours, (1944) 304
 - Subungual melanoma, (1940) 418
 - Succinylsulphathiazole, (1943) 52, 99, (1944) 113.
 - See also* Sulphasuxidine
 - dysentery treated with, (1944) 210
 - enteritis, infective, treated with, (1944) 60
- ## Sucrose
- clearance test, kidney function, of, (1940) 118
 - diuretic effect, (1940) 455
 - renal changes following intravenous hypertonic solutions of, (1940) 455
- ## Suction treatment of boils and carbuncles, (1941-2) 171
- ## Sudermo, (1943) 94
- ## Sugar-cane dust, bagassosis from inhalation of, (1944) 372
- ## Suicide, safeguarding of depressed patients from, (1944) 76
- ## Sulcus tumour of lung, (1941-2) 294
- ## Sulphacetamide, (1941-2) 113, (1943) 99
- ## Sulphadiazine, (1941-2) 6, 119, (1943) 5, 99, (1944) 114
- absorption, excretion, and distribution, (1941-2) 340
 - anuria following use of, (1943) 304
 - clinical applications, (1943) 306
 - efficacy, (1944) 327
 - gonorrhoea, in, (1944) 28
 - haematuria caused by, (1944) 245
 - infectious complications of diabetes mellitus, in, (1943) 187
 - infectious diseases, in, (1943) 55, 99
 - pneumonia, in, (1943) 99, 306
 - renal complications from use of, (1944) 328
 - spray, burns treated with, (1944) 172
 - therapy, (1941-2) 341
 - pneumonia, in, (1944) 332
 - toxicity, (1944) 327
 - urinary complications, (1943) 304
- ## Sulphaemoglobinaemia, sulphanilamide causing, (1940) 120
- ## Sulphaguandine, (1941-2) 6; (1943) 5, 99. *See also* Sulphanilylguanidine
- ## cholera, in, (1944) 100
- dysentery, bacillary, in, (1944) 101, 209, 210
 - infectious diseases, in, (1943) 55
 - recent work on, (1944) 113
 - therapy,
 - paratyphoid fever B, (1944) 224
 - typhoid fever, (1941-2) 222; (1944) 223
- ## Sulphamethazine, (1943) 5, 99; (1944) 114
- infectious diseases, in, (1943) 55
- ## Sulphamethylthiazole, (1941-2) 117
- boils treated with, (1940) 223
- ## encephalopathy following administration of, (1941-2) 175
- gonorrhoea treated with, (1941-2) 238

CUMULATIVE INDEX

Sulphamethylthiazole—continued

- polyneuritis, toxic, due to, (1943)*291
- properties of, (1940) 134, 461
- puerperal sepsis treated with, (1941-2) 370
- pyelitis treated with, (1940) 501
- staphylococcal infection, in, (1941-2) 342
- experimental, (1940) 461
- Staphylococcus aureus* infections, in, (1940) 134, 461
- toxic reactions, (1941-2) 343
- wounds, local application in, (1941-2) 267
- Sulphanilamide, (1939) 169, 174, 177, (1943) 5, 100
 - abortion fever, in, (1939) 183
 - actinomycosis, in, (1939) 186, (1940) 150
 - agranulocytosis caused by, (1939) 193
 - amidopyrine and, in pneumonias, (1940) 234
 - anaemia, secondary, produced by, (1941-2) 344
 - anthrax, in, (1940) 188
 - appendicitis, in, (1940) 190
 - aqueous and vitreous, presence in, (1940) 459
 - arthritis,
 - acute suppurative, in, (1940) 197
 - gonococcal, in, (1939) 226
 - B. coli* infections, in, (1939) 285; (1940) 133
 - bacteriostatic effect *in vitro*, (1940) 458
 - bites, human, in, (1941-2) 269
 - blood, preservation, use in, (1940) 219
 - brain abscess, in, (1939) 255
 - breast milk, in, (1939) 175, 357
 - excretion of, (1940) 458
 - bronchitis, in, (1940) 234
 - broncho-pneumonia, in, (1940) 234
 - Brucella abortus* infections, in, (1940) 133
 - chancreoid, in, (1941-2) 189
 - chemistry and pharmacology of, (1939) 169
 - children, in treatment of, (1939) 41
 - Cl. welchii* infections, in, (1940) 133; (1941-2) 341
 - colitis, ulcerative, in, (1939) 288; (1941-2) 194
 - concentration of, adequate, (1940) 133
 - conjunctivitis, in, (1940) 251
 - inclusion, (1941-2) 196
 - corneal ulcer, in, (1940) 253
 - cyanosis caused by, (1939) 295
 - cystitis, in, (1939) 243, (1940) 208
 - dermatitis, streptococcal, in, (1940) 532
 - dermatoses, pyogenic, in, (1940) 260
 - dosage, (1940) 133
 - drug fever, second attack of, due to, (1940) 459
 - endocarditis, malignant, in, (1939) 369
 - erysipelas, in, (1939) 335, (1940) 297, (1941-2) 224
 - ethyl-sulphonate, M 541, (1940) 133
 - fluid intake during treatment with, (1940) 133
 - fractures, in, (1941-2) 210
 - gas gangrene, in, (1941-2) 341
 - gonococcal infections, in, (1940) 133
 - ophthalmia, (1939) 291, (1940) 251
 - gonorrhoea, in, (1939) 357-9, (1944) 28
 - haemoglobinuria caused by, (1941-2) 240
 - healing wounds, effect on, (1939) 386
 - hypersensitivity to, following X-ray therapy, (1940) 505
 - infectious diseases, in, (1943) 55
 - intestinal obstruction, in, (1941-2) 272
 - intrapertoneal, (1941-2) 272
 - jaundice, use in presence of, (1940) 359
 - laryngo-tracheobronchitis, in, (1941-2) 281
 - liver necrosis and, (1941-2) 343
 - local therapy, wounds, (1941-2) 266, (1944) 270
 - lymphopathia venereum, in, (1940) 398
 - mastoiditis, in, (1939) 324
 - mechanism of, (1943) 5
 - meningitis,
 - meningococcal, in, (1939) 17, 88, 429
 - pneumococcal, in, (1939) 88, 427; (1943) 280
 - pyogenic, in, (1939) 88, 428
 - meningococcal infections, in, (1940) 133
 - myopia caused by, (1941-2) 310
 - nicotinic acid with, (1940) 129
 - ophthalmia,
 - gonococcal, in, (1940) 251
 - neonatorum, in, (1939) 291
 - osteomyelitis, acute, in, (1941-2) 172

Sulphanilamide—continued

- otitis media, in, (1939) 323; (1941-2) 216
- paste preparations, (1943) 100, 305
- peritonitis, in, (1940) 190, 443
- pharyngitis, streptococcal, in, (1940) 463
- placental transmission, (1939) 357; (1940) 458
- pneumococcus, action on, (1940) 133
- powder, obstetric and gynaecological operations, in, (1944) 25
- preservative for blood, as, (1941-2) 169
- proteolytic products, influence of, on effectiveness, (1940) 458
- puerperal sepsis, in, (1940) 499
- pyelitis, (1939) 508
 - pregnancy, of, in, (1940) 501
- pyogenic dermatoses, in, (1940) 260
- rashes, (1939) 319
- rectal administration, (1941-2) 343
- rheumatic
 - fever, in, (1943) 327
 - infection, acute, in, (1941-2) 378
- rheumatism,
 - acute, in, (1939) 523
 - effect on, (1939) 140
- scarlet fever, in, (1939) 526
- spermatogenesis, effect on, (1940) 543
- staphylococcal infection, in, (1941-2) 342
- streptococcal septicaemia, in, (1939) 530
- surgical infection, in, (1939) 25
- thrombosis, lateral sinus, in, (1943) 362
- toxic effects, (1941-2) 240
- toxic hepatitis during administration of, (1939) 409
- trachoma, in, (1941-2) 412
- tularaemia, in, (1940) 569
- urethritis, in, (1939) 584
- urinary tract infections, in, (1940) 208, (1941-2) 344
- vitreous and aqueous, presence in, (1940) 459
- whooping-cough, in, (1939) 605
- Sulphanilylbenzamide, (1943) 99
- Sulphanilyldimethylsulphanilamide, ophthalmia, epidemic gonorrhoeal, treated with, (1943) 178
- Sulphanilylguanidine, (1941-2) 119, (1943) 99. *See also* Sulphaguanidine
- dysentery treated with, (1941-2) 65
- bacillary, (1941-2) 213, (1943) 85
- Sulphapyrazine, pneumonia treated by, (1943) 311
- Sulphapyridine, (1943) 5, 100 *See also* Sodium sulphapyridine
- abortion fever, in, (1940) 143
- administration, (1940) 134
- agranulocytosis caused by, (1940) 156, (1941-2) 134, 343
- anaemia, haemolytic, caused by, (1940) 120
- anthrax, in, (1940) 188, (1943) 128
- anuria due to, (1941-2) 161, (1944) 278
- barbiturates used with, (1940) 472
- bronchiectasis, in, (1940) 234
- calculi, causing, (1941-2) 161
- renal, (1940) 367
- cerebrospinal fever, in, (1940) 134, (1941-2) 187, (1944) 177
- children's diseases treated with, (1941-2) 48
- dermatitis, exfoliative, in, (1940) 260
- dermatoses, in, (1941-2) 342
- dysentery, bacillary, in, (1941-2) 118
- empyema, tuberculous, in, (1940) 286
- endocarditis, bacterial, in, (1941-2) 118
- heparin and, (1941-2) 251
- subacute, (1940) 334; (1941-2) 251
- excretion of, (1940) 459
- glandular fever, in, (1940) 313, (1941-2) 118
- gonococcal infections, in, (1940) 134
- gonorrhoea, in, (1940) 90, 318; (1941-2) 117, 237; (1943) 91, (1941) 243
- granuloma, ulcerative, in, (1941-2) 239
- haematuria caused by, (1940) 324, 367
- herpes labialis caused by, (1943) 242
- hypodermoclysis, advantages of, (1940) 460
- hypopyon corneal ulcer, in, (1941-2) 198
- infectious diseases, in, (1943) 55
- injection of, (1940) 135
- kidneys, effect on, (1944) 329
- laryngo-tracheobronchitis, in, (1941-2) 281
- leukaemia, lymphocytic, in, (1941-2) 286

CUMULATIVE INDEX

Sulphapyridine—continued

- lung abscess, in, (1941-2) 290
- lupus erythematosus, in, (1940) 396; (1941-2) 118
- lymphopathia venereum, in, (1940) 398
- meningitis,
 - influenzal, in, (1940) 404; (1941-2) 304
 - meningococcal, in, (1940) 134
 - pneumococcal, in, (1940) 402-4, (1941-2) 304; (1943) 280
 - pyogenic, in, (1941-2) 304
- meningococcal infections, in, (1940) 134
- myopia caused by, (1941-2) 310
- ophthalmia neonatorum, in, (1941-2) 196
- patent ductus arteriosus, infected, in, (1943) 233
- periphagus neonatorum, in, (1940) 436
- peritonitis, in, (1940) 443
- plague, in, (1943) 85
- pneumococcal infections, in, (1940) 133, (1941-2) 342
- pneumonia, in, (1940) 469-73; (1941-2) 177, 431
 - hydroxyethylapocupreine dihydrochloride and, (1940) 472
 - lobar, (1941-2) 353
 - poliomyelitis, in, (1941-2) 356
 - porphyrin excretion, effect on, (1940) 120
 - procaine hydrochloride, injection of, (1940) 135
 - psittacosis, in, (1941-2) 361
 - ray therapy, and, (1940) 505
 - renal calculi due to, (1943) 257
 - Ritter's disease, in, (1940) 260
 - saliva, excretion in, (1940) 459
 - septicaemia, in, (1940) 519
 - serum and, in pneumonia, (1940) 472
 - skin lesions, generalized, caused by, (1941-2) 213
 - soluble, (1940) 471
 - staphylococcal infection, in, (1940) 134, 461, 519, (1941-2) 342
 - Streptococcus viridans*, effect on, (1940) 134
 - tetanus, in, (1941-2) 118, 407
 - thrombocytopenic purpura caused by, (1941-2) 343
 - toxic effects, (1940) 456, (1941-2) 134, 213, 343, (1944) 329
 - relative toxicities of sulphanilamide and sulphapyridine, (1940) 460
 - trachoma, in, (1940) 564, (1941-2) 412
 - tubercle bacillus, effect on, (1940) 457
 - tuberculosis, in, (1941-2) 415
 - pulmonary, (1940) 390
 - typhoid fever, in, (1940) 290
 - undulant fever, in, (1940) 143
 - ureters, blockage of, caused by, (1940) 369
 - urinary tract complications due to, (1941-2) 346
 - Vibrio septique*, effect on, (1940) 134

Sulphasuxidine, infectious diseases, in, (1943) 52, 55

See also Succinylsulphathiazole

Sulphathiazole, (1941-2) 6, (1943) 5, 100

 - agranulocytosis caused by, (1941-2) 134
 - boils and carbuncles, in, (1941-2) 171
 - calculi, urinary, caused by, (1940) 367
 - cerebrospinal fever, in, (1941-2) 187
 - clinical applications, (1941-2) 116
 - contra-indications, (1943) 307
 - diabetes mellitus, infectious complications of, in, (1943) 187
 - diarrhoea, infantile, in, (1941-2) 208, (1943) 188
 - eczema treated with, (1943) 199
 - endocarditis, bacterial, in, (1941-2) 118
 - general action, (1941-2) 340
 - gonorrhoea,
 - females in, (1943) 91, 226; (1944) 28
 - males, in, (1941-2) 237, (1944) 243
 - treated with, (1941-2) 107; (1944) 107
 - haematuria caused by, (1940) 367, (1941-2) 240
 - infectious diseases, in, (1943) 55
 - inhalations, prophylactic effects of, (1944) 328
 - local application of, (1940) 133; (1941-2) 114
 - malaria therapy, effect on rigors in, (1941-2) 301
 - microcrystals of, (1944) 121
 - osteomyelitis and pericarditis treated with, (1941-2) 49
 - otolaryngology, use in, (1944) 121
 - plague treated with, (1940) 468; (1943) 85

Sulphathiazole—continued

- pneumococcal infections, in, (1940) 134
 - pneumonia, in, (1940) 473; (1941-2) 177
 - lobar, (1941-2) 352-4
 - properties of, (1940) 461
 - pyclitis treated with, (1940) 501
 - recent work on, (1944) 113
 - renal complications, (1941-2) 343
 - renal tubules, concretions in, due to, (1940) 461
 - septicaemia, in, (1940) 519
 - sinusitis, in,
 - acute, (1944) 121
 - chronic, sodium salt of sulphathiazole in, (1941-2) 127
 - skin, conjunctival and scleral reactions, (1940) 460
 - snuff,
 - antiseptic, as, (1941-2) 331
 - carriers of *C. diphtheriae* treated with, (1943) 100, 171
 - nasal infections, for, (1943) 100, 305
 - spine, osteomyelitis of, in, (1941-2) 397
 - staphylococcal
 - bacteraemia and septicaemia, in, (1943) 332
 - infection, in, (1940) 3, 134, (1941-2) 342
 - Staphylococcus aureus* infections, in, (1940) 461
 - streptococcal infections, in, (1940) 134, 519
 - therapeutic use of, (1940) 134
 - toxic effects, (1940) 460, (1941-2) 134, 238, 240, (1943) 307, (1944) 384
 - administration of *p*-aminobenzoic acid, (1941-2) 344
 - urinary tract,
 - complications due to, (1941-2) 346
 - infection, in, (1941-2) 344, (1943) 307
 - vulvo-vaginitis, in, (1943) 91
 - wound healing, effect on, (1944) 269
- Sulphonamide drugs, (1941-2) 6, 114, (1943) 5, 54, 62, 72, 81, 98, 304, (1944) 13
- Sulphonamides
- abortion, incomplete, in, (1941-2) 126
 - abortion fever treated with, (1939) 183
 - absorption, distribution and excretion, (1939) 174, (1941-2) 340, (1943) 304
 - actinomycosis, in, (1941-2) 118, 129
 - action, mode of, (1939) 172, (1944) 111
 - agranulocytosis caused by, (1939) 32, 177
 - albumic, (1939) 171, (1940) 133, 319
 - antibodies, specific, (1939) 172
 - anti-endotoxic action, (1939) 172
 - anuria,
 - caused by, (1944) 396
 - complicating therapy, (1941-2) 108
 - arthritis, in, (1939) 229
 - gonococcal, (1940) 91, 197
 - asthma, bronchial, in, (1943) 138
 - aural infections, in, (1941-2) 118
 - bacteria, effect on, (1939) 173
 - B. coli* infections treated with, (1941-2) 100
 - benzylsulphanilamide, (1940) 133
 - body fluids, estimation in, (1939) 173
 - breast milk, in, (1939) 33
 - bubonic plague, in, (1941-2) 99
 - burns, in, (1943) 167, 305
 - glycerin-sulphonamide paste, (1941-2) 182
 - powder, (1941-2) 180
 - cavernous sinus, in,
 - thrombophlebitis, (1941-2) 408
 - thrombosis, (1943) 14
 - cerebrospinal fever, in, (1940) 244; (1941-2) 65; (1943) 172, (1944) 177-9
 - chancroid, in, (1940) 91, 245, (1944) 106
 - child, dosage and tolerance in, (1941-2) 48
 - children's diseases, in, (1941-2) 48
 - dosage, (1940) 456
 - Cl. welchii* infections, action on, (1939) 171
 - clinical applications, (1941-2) 116
 - colitis, ulcerative, in, (1941-2) 194
 - complications, dosage and clinical uses, (1943) 304
 - conjunctivitis, allergic, caused by, (1944) 186
 - cutaneous eruptions caused by, (1941-2) 344
 - cyanosis caused by, (1939) 176; (1940) 120, 133, 457; (1941-2) 115
 - dermatitis caused by, (1940) 257

CUMULATIVE INDEX

Sulphonamides—continued

dermatoses, pyogenic, in, (1944) 199
 4:4'-diaminodiphenylsulphone, (1939) 171
 diseases treated with, (1939) 17
 dosage, (1939) 177
 dysentery, in, (1941-2) 65
 bacillary, (1941-2) 118
 endocarditis,
 bacterial, in, (1939) 171; (1941-2) 118
 subacute bacterial, in, (1940) 334-6, (1943) 237;
 (1944) 249
 enteric fevers, in, (1939) 330
 E.O.S., (1943) 5, 100, 307
 erysipelas, in, (1939) 335
 exanthemata, in, (1939) 79
 excretion, (1939) 175, (1941-2) 116
 eye infections, in, (1944) 328
 gas gangrene, in, (1940) 309
 gonorrhoea, (1939) 155, 171, 357; (1940) 90,
 319; (1941-2) 107, (1943) 91, (1944) 28,
 107
 females, in, (1941-2) 117
 males, in, (1940) 319; (1944) 243
 haematuria and renal colic due to, (1941-2) 116
 haemoglobin metabolism and hepatic function,
 effect on, (1940) 458
 haemolytic anaemia caused by, (1939) 177
 host, action on, (1939) 172
 hyperpyrexia caused by, (1939) 176
 hypopyon corneal ulcer, in, (1941-2) 198
 impetigo, in, (1943) 246, (1944) 256
 infectious diseases, in, (1943) 54
 kidneys, effects on, (1940) 457
 leishmaniasis, cutaneous, treated with powdered,
 (1940) 378
 leucocytes, effect on, (1939) 172
 leukaemoid reactions due to, (1941-2) 285
 local application of, (1940) 10, 132, 351; (1941-2)
 114
 eye infections, in, (1944) 328
 nerve paralyses after, (1944) 312
 peritonitis, in, (1941-2) 13
 wounds, in, (1941-2) 266
 infected, (1944) 268
 lupus erythematosus, in, (1940) 395, (1941-2) 118,
 299
 lymphogranuloma
 inguinale, in, (1939) 155, (1941-2) 109
 venereum, in, (1943) 227
 lymphopatia venereum, in, (1941-2) 300
 M 541, (1940) 133
 M & B 693, (1939) 171, 173-5, 177 *See also*
 Sulphapyridine
 M & B 760, (1940) 134. *See also* Sulphathiazole
 malaria, in, (1940) 76
 measles, in, (1944) 299, 300
 meningitis, in, (1941-2) 58
 pneumococcal, action on, (1939) 171, 427,
 (1941-2) 304
 pyogenic, (1939) 88, 428
 meningococcus, action on, (1939) 170
 middle-ear disease, complications of, in, (1939)
 88
 nervous symptoms caused by, (1939) 177
 neutralizing effect on metabolic factor, (1939)
 173
 new compounds, (1941-2) 119; (1943) 98-100
 ocular infection, in, (1941-2) 118
 ointments, (1941-2) 115
 dermatoses, pyogenic, treated with, (1944) 199
 ophthalmology, in, (1941-2) 342, (1943) 147, 179
 oriental sore, in, (1940) 378, (1944) 284
 otitis media, in, (1944) 219
 acute, (1940) 284; (1941-2) 57
 otology and laryngology, in, (1941-2) 56
 peritoneum, effects on, (1943) 305
 phagocytes, effect on, (1939) 172
 pharmacology of, (1939) 169; (1941-2) 115, 340
 plague, in, (1943) 85
 pneumococcal infection, in, (1941-2) 342
 pneumococcus, action on, (1939) 171, 173, 175;
 (1941-2) 342
 pneumonia, in, (1939) 16, 480; (1940) 234, 469-73;
 (1941-2) 177; (1943) 306
 lobar, (1941-2) 352

Sulphonamides—continued

poliomyelitis, in, (1941-2) 49
 porphyrin excretion following, (1940) 324
 prontosil, rubrum and soluble, (1939) 169
 prontosil, (1939) 170
 prosectasine, (1939) 170; (1940) 133
 proseptine, (1939) 170
 puerperal sepsis, in, (1939) 31, (1941-2) 370
 pulmonary infections, in, (1939) 115
 pyelitis, in, (1939) 508
 pyelephlebitis, in treatment of, (1940) 12
 rashes caused by, (1941-2) 344
 recent work on, (1940) 132; (1944) 111
 renal lesions caused by, (1940) 457
 resistance, (1944) 112
 respiratory diseases, in treatment of, (1940) 6
 rheumatic fever treated with, (1941-2) 49
 rodilone, (1940) 134
 rubiazol, (1939) 170; (1940) 133
 scarlet fever, in, (1940) 514
 septicaemia, in, (1940) 12, 519; (1941-2) 58, 115
 skin lesions, (1943) 305
 skin reactions, (1939) 176
 sodium compounds, (1941-2) 340
 urinary tract complications due to, (1941-2)
 346
 soft chancre, in, (1939) 155
 soluseptasine, (1939) 170, (1940) 133
 staphylococcal infections, action on, (1939) 171,
 (1940) 3
 streptocide, (1939) 170
 streptococcal infections, in, (1940) 3, 12, 133, 532,
 571
 streptococcus, haemolytic, action on, (1939) 170,
 173
 sulphanilamide. *See* Sulphanilamide
 sulphapyridine. *See* Sulphapyridine
 sulphathiazole. *See* Sulphathiazole
 sulphonamide-P, (1939) 170
 sulphur-containing substances, and, (1941-2) 346
 surgery, application to, (1940) 12
 tetanus, in prophylaxis of, (1940) 10
 thiazamide, (1940) 134
 thrombosis, septic, in, (1941-2) 59
 tonsillitis, acute, in, (1941-2) 60
 toxic effects of, (1939) 13, 176, (1940) 456, 460;
 (1941-2) 6, 115, 310, 343, (1944) 245, 396
 agranulocytosis, (1943) 109
 anaemia, acute haemolytic, (1943) 118
 anuria, (1944) 278
 childhood, in, (1941-2) 48
 dermatitis, (1940) 257, (1943) 183
 polyneuritis, (1943) 291
 relative, (1941-2) 116
 renal calculi due to, (1943) 257
 urinary complications, (1943) 304
 toxicity, (1944) 384
 tracheo-bronchitis, (1941-2) 412
 trachoma, in, (1939) 574, (1940) 564; (1941-2)
 412
 tropical diseases, in, (1941-2) 99, 344
 tropical ulcer, in, (1940) 565
 tubercle bacillus, effect on, (1940) 457
 tuberculosis, in, (1940) 95, 390, 568
 tularaemia, in, (1943) 369
 uleron, (1939) 171, 174
 undulant fever, in, (1939) 584, (1940) 573; (1941-2)
 100
 ureters, blockage of, caused by, (1940) 369
 urinary
 antiseptics, as, (1941-2) 117
 calculi caused by, (1944) 329
 urinary infection, in, (1943) 307
 urine, and, (1940) 457, 459
 vulvo-vaginitis, in, (1940) 91
 wounds, in, (1940) 10, 132, 351, (1941-2) 114,
 (1943) 9, 170, 305
 infected, (1941-2) 265
 war, (1941-2) 10; (1944) 111
 Sulphonated oil, detergent in dermatitis venenata,
 as, (1941-2) 203
 Sulphur
 colloidal, rheumatoid arthritis, in, (1940) 198
 iodized, in arthritis, (1940) 200
 hypertension, in, (1940) 214

CUMULATIVE INDEX

- Sulphur**—*continued*
 iodine, and, in rheumatoid arthritis, (1939) 227
 scabies, in, (1943) 342
Sulphur-containing substances and sulphonamides, (1941-2) 346
Sulphydryl compounds, effect on wound healing, (1941-2) 113
Sunshine, bright, arcus senilis caused by, (1939) 293
Supradiaphragmatic splanchnectomy, essential hypertension, in, (1941-2) 164
Suprarenal cortex extract, (1943) 94
 Addison's disease with diabetes mellitus, in treatment of, (1943) 106
Supraspinatus tendon, calcification in, (1941-2) 189
Suprasternal bone, (1941-2) 371
Supratentorial lesions, diagnosis by olfactory tests, (1944) 65
Supravital staining of leucocytes, (1941-2) 7
Suramin, (1940) 127; (1941-2) 112
Surfer's feet, bacteriology and treatment of, (1939) 343
Surgery
 advances in, (1941-2) 8; (1943) 8; (1944) 13
 aged, of the, (1941-2) 380; (1943) 12
 air-raid casualties, of, (1941-2) 265
 alcoholism, chronic, in surgical patients, (1940) 158
 anaesthesia, (1939) 25
 cancer, surgical treatment of, (1939) 28
 cardiac, (1943) 13
 diagnosis, (1939) 23
 general, (1939) 23; (1944) 13
 hippuric acid test in, (1944) 287
 intramuscular injection of fluids, (1940) 348
 ophthalmic, (1943) 81
 plastic, (1941-2) 12
 regional, (1944) 19
 reparative or restorative, (1941-2) 12
 special organs, of, (1939) 26
 ultra-violet rays, filtered, in, (1940) 150
 vitamin C in relation to, (1940) 589
 war, (1940) 9, (1941-2) 8, (1943) 8, (1944) 16 9
Suture
 coagulated blood plasma in nerve, (1941-2) 264
 fibrin, for repair of divided nerve, (1944) 311
 ligatures and, (1939) 26
 material, (1944) 15
 silk, in infected wounds, (1941-2) 266
 synthetic plastic, (1941-2) 264
Svedborg ultra-centrifuge, (1940) 121
Swallowing
 mechanism of, (1944) 121
 nervous disorders of, (1944) 218
 sweat glands, tumours derived from, (1944) 374
Swine influenza
 aetiology, (1944) 40
 reservoir of the virus, (1944) 40
Sympathectomy
 angina pectoris, in, (1940) 184
 arteriosclerotic endarteritis treated by, (1944) 151
 cervico-thoracic, for acrocyanosis, (1941-2) 226
 clinical applications of, (1939) 552
 hypertension, essential, in, (1944) 160
 obliterative vascular disease, for, (1943) 134
 thrombo-angitis obliterans, in (1939) 225
Sympathetic nervous system *See also Autonomic nervous system*
 denervation of arm, (1944) 81
 innervation of upper extremities, (1944) 82
 peptic ulcer, role in, (1944) 318
 tumours, (1943) 354, (1944) 381
Sympathetic and parasympathetic nervous system, (1939) 552
 hormones and drugs, action of, (1939) 552
 renal sympathetico-tonus, (1939) 552
Sympathetico-adrenal mechanism in migraine, (1943) 280
Sympathogonioma, anterior superior mediastinum, of, (1944) 381
Sympathomimetic and parasympathomimetic drugs, intravenous drip administration, (1941-2) 346
Sympatol, (1939) 164
Synapoidin, (1941-2) 22
Syncope, cardiac, atropine-adrenaline-strophanthine mixture in, (1940) 509
Syndrome
 Adams-Stokes, (1941-2) 246
 Adie's, (1944) 149
 adrenogenital, (1944) 54
 Albright's, (1944) 162
 band-shaped keratitis and arthritis, (1943) 180
 Banti's, (1941-2) 398
 carotid sinus, (1943) 354
 cerebro-retinal, (1943) 172
 cervico-brachial, (1943) 173
 crush, (1941-2) 9, 269; (1941-2) 1; (1943) 19, 249
See also Crush syndrome
 Da Costa's, (1941-2) 2, 244; (1943) 231
 effort, (1941-2) 2, 46, 244; (1943) 68, 231. *See also Effort syndrome*
 Ehlers-Danlos, (1941-2) 230; (1943) 212
 emotion, (1944) 340
 Felty's, (1944) 152
 Guillain-Barré, (1941-2) 315; (1943) 291
 Hand-Schüller-Christian. *See Schüller-Christian*
 hepato-renal, (1944) 229
 ileo-gastric, (1944) 147
 Kleine-Levin, (1943) 318
 Korsakow's, (1941-2) 369
 Laurence-Moore-Biedl, (1941-2) 162, 351
 Libman-Sacks, (1943) 348
 Löffler's, (1941-2) 157
 Maffucci's, (1944) 162
 Marchiafava-Micheli, (1941-2) 140
 Marfan's, (1943) 159
 'mega', (1944) 85
 Meigs's, (1944) 314
 Ménière's, (1941-2) 422, (1943) 38, 376, (1944) 404
 menopausal, (1943) 175
 morphine abstinence, (1943) 196
 nephrotic, (1943) 31, 288
 hypertension, with, in diabetes mellitus, (1941-2) 205
 Parinaud's oculo-glandular, (1941-2) 109
 Paterson's, (1941-2) 128
 Plummer-Vinson, (1941-2) 128, (1943) 104
 post-concussional, (1944) 185
 Raynaud's, (1944) 82
 Rendu-Osler, (1941-2) 223
 scalenus, (1941-2) 189
 Schüller-Christian, (1941-2) 287, (1943) 266
 Simmonds's, (1941-2) 390, (1943) 339, (1944) 45
 sprue, (1941-2) 26
 Turner's, (1943) 197
 van der Hoeve's, (1943) 204
 Waterhouse-Friedrichsen, (1941-2) 132, 180
 Weber-Christian, (1943) 208
 Werner's, (1943) 298
 Wolff-Parkinson-White, (1943) 131
Synovial membrane
 tumours of, (1940) 361, (1941-2) 274, (1943) 256
 granuloma, traumatic, (1941-2) 274
 knee, glomus, (1941-2) 393
 synovioma, malignant, (1940) 361, (1941-2) 274, (1943) 256
Synthalin
 kala-azar, in, (1940) 78
 protozoal infections, in, (1940) 78
 trypanosomiasis, in, (1940) 78
Syntrogl, peptic ulcer treated with, (1941-2) 327
Syntropan
 megacolon, in, (1939) 426
 Parkinsonism, in, (1941-2) 220
Syphilid, nodular, of face, (1941-2) 403
Syphilis, (1939) 151, 553, (1941-2) 102, 403; (1943) 87, 355
 acquired, (1941-2) 403
 prognosis, (1939) 554
 tertiary, (1939) 555
 aetiology, (1941-2) 403
 aneurysm caused by, (1941-2) 143
 aortic valve lesion due to, (1943) 238
 aortic valvular change due to, (1941-2) 249
 bacteriology, (1940) 87
 blindness due to, (1940) 210

CUMULATIVE INDEX

Syphilis—continued

- blood,
 - cytology of, (1941-2) 102
 - plasma, survival of *S. pallida* in, (1944) 102
 - transfusion and, (1940) 210
- cardiovascular, (1940) 5; (1943) 238, 239
- children, death-rate among, from, (1939) 40
- congenital, (1939) 555; (1941-2) 403
 - clavicle, enlargement of inner end of, (1939) 555
 - diagnosis in still-born, (1943) 89, 356
 - heart disease, incidence of, (1941-2) 403
 - Parrot's pseudo-paralysis, (1941-2) 404
 - prevention, (1944) 382
 - rhagades, (1941-2) 403
 - teeth, (1944) 382
 - treatment, (1944) 382
 - prenatal and postnatal, (1943) 358
 - unusual manifestations, (1941-2) 404
- conjugal neurosyphilis, (1941-2) 403
- diagnosis, (1940) 88, 547; (1941-2) 102; (1943) 355
 - Kahn verification test, (1941-2) 103, (1943) 88, 355
 - Kolmer test, modified, (1940) 547
 - laboratory tests, (1939) 151, 553; (1940) 547
 - Laughlin test, (1940) 210
 - Meinicke flocculation test, (1940) 547
 - microscopical examination, (1939) 151
 - serum tests, (1939) 554, (1940) 88, 547, (1941-2) 103, (1943) 87, 355
 - complement fixation, (1939) 554
 - false positive reactions, (1943) 87, 355; (1944) 102
 - Kline precipitation, (1939) 554
 - leprosy and malaria reactions simulating, (1943) 355
 - quantitative method, value of, (1944) 104
- Wassermann and Meinicke flocculation tests, (1940) 547
 - Boerner-Lukens modification of Wassermann test, (1940) 547
- gastric, (1941-2) 234
- heart, of, (1943) 238
 - hypertension, in, and, (1943) 239
- incidence, (1943) 87, 358
- infection, extragenital, (1941-2) 403
- infection with other organisms, resistance to, (1941-2) 104
- infectivity,
 - age of infection, and, (1941-2) 102
 - early and late lesions, of, (1944) 382
 - vaginal and uterine secretions, of, (1941-2) 102
- intraocular, (1940) 425, (1941-2) 315, (1943) 292
- nephritis occurring in, (1940) 421
- nodular syphilide of face, (1941-2) 403
- old age, in, incidence of, (1941-2) 380
- optic atrophy due to, (1940) 210
- pregnancy, in, (1944) 24
- prognosis, (1941-2) 104
- prostitutes, in, (1944) 382
- pulmonary aneurysm due to, (1944) 139
- rupial, (1940) 548
- secondary, (1941-2) 403
- skin, of, (1939) 64
 - psoriasis, resembling, (1941-2) 403
 - spirochaetes,
 - identification of, (1939) 554
 - staining of, (1939) 553
- stomach, of, (1941-2) 234
- S. pallida*, cultivation of, (1943) 87
- tertiary, (1941-2) 403
- treatment, (1939) 555; (1941-2) 104, 404; (1943) 89, 356
 - acetarsol, (1939) 556
 - acetarsone, (1941-2) 404
 - acetylglucarsenobenzene, (1941-2) 404
 - anti-syphilitic, petechial haemorrhage caused by, (1941-2) 405
 - arsenical compounds, (1941-2) 105, 404
 - arsenotherapy, massive, (1939) 555; (1943) 89, 357, (1944) 105
 - arsenoxide, (1941-2) 105
 - arsphenamine in, (1940) 87
 - side effects, (1939) 557; (1940) 549

Syphilis—continued

- treatment—continued
 - bismuth,
 - cervico-vaginitis due to, (1940) 550
 - elimination of tissue deposits by ammonium chloride, (1941-2) 404
 - jaundice complicating, (1939) 557
 - concurrent versus alternating arsenical and heavy metal treatment, (1944) 105
 - continuous, (1940) 549
 - five-day, (1941-2) 104; (1943) 356-9
 - heat, (1941-2) 105
 - intravenous drip method, (1940) 90
 - arsenotherapy, (1943) 356, 359
 - chemotherapy, (1940) 548
 - liver injury, in, (1940) 549
 - mapharsen, (1940) 548-50
 - mapharside, (1939) 556; (1940) 90; (1941-2) 404
 - massive-dose therapy, results of, (1943) 90, 357
 - mercury, healing of obstructive lesions, (1941-2) 404
 - methods, comparison of, (1943) 357
 - neoarsphenamine, (1940) 87, 90
 - prevention, (1940) 87
 - arsenoxide in, (1940) 87
 - mapharside in, (1940) 87
 - prophylactic, prenatal, (1943) 355
 - pyretotherapy, (1943) 90
 - pyrexia, artificial, in, (1941-2) 105
 - results, evaluation of, (1943) 357
 - side effects, (1941-2) 405
 - subisminol mass, (1940) 548
 - thiosulphate on excretion of arsenic, effect of, (1941-2) 404
 - war-time, in, (1943) 87, 358
 - Syphilitic
 - aortic valvulitis, (1943) 238
 - aortitis, (1943) 134
 - Syphiloma, diffuse hypertrophic, (1940) 398
 - Syngomyelia
 - painless paronychia in, (1939) 441
 - tabes dorsalis and, (1940) 425
 - Systolic
 - "clicks", spontaneous pneumothorax, in, (1940) 474
 - gallop rhythm, mechanism of, (1940) 192
- T
- T A.B. vaccine. *See* Vaccines
 - T A B C. vaccine, (1941-2) 261
 - Tabes dorsalis
 - bladder symptoms, (1940) 425
 - brain tumour, diagnosis from, (1939) 260
 - gastric crises, anterior chordotomy for, (1940) 426
 - syngomyelia associated with, (1940) 425
 - treatment of, (1939) 448
 - vitamin E in, (1940) 131
 - Tabetic
 - cord bladder, (1940) 425
 - crises, chordeotomy, anterior, for, (1940) 426
 - Tachycardia
 - diagnosis, (1940) 191
 - electrocardiographic changes during induced fever, (1943) 131
 - paroxysmal,
 - electrocardiographic observations, (1944) 150
 - symptoms, (1941-2) 150
 - Wolff-Parkinson-White syndrome, (1943) 131
 - quinidine in, (1939) 223
 - sign of the unbalanced pendulum, (1940) 191
 - Takata-Ara reaction, (1939) 246, (1940) 386
 - Talipes, (1939) 558
 - adhesive plaster treatment, (1939) 558
 - Tannic acid
 - burns treated with, (1940) 10, 236-9; (1941-2) 179, 181
 - children, in, bath treatment of, (1939) 268
 - ferric chloride, and, (1939) 269
 - Tapeworm infections, intestinal, (1939) 558
 - atropine sulphate in, (1939) 558
 - Diphyllobothrium latum*, (1939) 558
 - gastric juice, influence of, (1939) 558
 - liver extract treatment, effect on, (1939) 558

CUMULATIVE INDEX

- Tarsus, tuberculous, treatment of, (1941-2) 274
Tattoo, mercury sulphide, for leucoplakia vulvae, (1941-2) 430
Tea drinking, effects of, (1940) 462
Teeth
 calcification, vitamin D and, (1940) 130
 caries, vitamin D and, (1940) 130
 carious, dental hypoplasia and, (1944) 196
 defects and alopecia, (1943) 113
 development, malnutrition and, (1944) 196
 diet and, (1940) 257
 estimation of age from, (1941-2) 303
 extraction,
 neurological complications, (1941-2) 202
 stammering cured by, (1944) 376
 gastric disorders, relation to, (1944) 31
 healthy, causes of, (1940) 257
 Hutchinson's, in non-syphilitics, (1941-2) 202
 hyperparathyroidism, in, (1941-2) 322
 hypoplasia and caries, (1944) 196
 industry, importance of oral hygiene in, (1944) 386
 noxious agents, effects of, (1944) 386
 school children's, care of, (1944) 196
 syphilis, congenital, in, (1944) 382
Telangiectases, associated with pregnancy, (1943) 205
Telangiectasia
 familial haemorrhagic, associated haemorrhages, (1941-2) 223
 hereditary, with visceral involvement, (1941-2) 223
Teleradium therapy
 larynx, in cancer of, (1944) 283
 rhinoscleroma, in, (1940) 512
Temperament, constitution and, (1944) 77
Temperature
 basal body, at time of ovulation, (1944) 26
 low, cancer treated by, (1941-2) 184
Temporal arteritis, (1941-2) 152, (1943) 131
Temporal
 artery,
 inflammation of, (1941-2) 152
 thrombosis of, (1941-2) 152
 bone, fractures, (1940) 49-53
 Schuller-Christian syndrome involving, (1941-2) 287
 loose,
 lesions of, (1940) 229
 directional preponderance of nystagmus in, (1944) 88
Tendon
 anterior commissure, (1943) 263
 injuries of, (1941-2) 265
 reflexes, heredo-familial areflexia without pupillary changes, (1940) 507
 supraspinatus, calcification in, (1941-2) 189
Teno-synovitis, De Quervain's, (1940) 329
Teratoma, testis, of, concurrent seminoma, (1941-2) 405
Terpinol, (1943) 96
Test
 Aschheim-Zondek, modification of, (1940) 478
 Boerner-Lukens modification of Wassermann, (1940) 547
 bromsulphalein, serial, (1944) 288
 cephalin-cholesterol flocculation, (1944) 288
 cold-pressor, in pregnancy, (1940) 479
 collargol, (1941-2) 188
 colloidal-gold reaction, (1940) 386
 complement fixation, for malaria, (1943) 83
 dark-adaptation, (1940) 585
 Dick, (1941-2) 261
 exercise tolerance, (1941-2) 44, 244
 flying aptitude, (1941-2) 29
 Frei, (1943) 92
 Friedman, (1940) 246, 478, 481
 galactose tolerance, (1940) 385
 Hamilton-Schwartz, (1943) 298
 hippuric acid, (1940) 386, (1944) 287
 Holmgren wool, (1940) 60
 hydrochloric acid and collargol, (1941-2) 188
 intelligence, in cases of brain injury, (1940) 60
 Ito-Reenstierna, (1940) 91
 Kahn, (1941-2) 103; (1943) 88, 355
Test—continued
 kidney function, of. *See* Kidney, function tests
 Knox cube, (1940) 61
 Kohs-Block, (1940) 60
 Kolmer, modified, (1940) 547
 lepromin, (1944) 284
 Levinson's, in tuberculous meningitis, (1940) 405
 liver function, (1940) 385-7, (1941-2) 4; (1943) 267, (1944) 286-9. *See also* Liver function test
 Mantoux, (1940) 568, (1941-2) 292
 meal, perforation of duodenal ulcer following, (1940) 438
 Meinicke flocculation, (1940) 547; (1941-2) 414
 ovulation, for, (1944) 25
 Paul-Bunnell, (1941-2) 235, (1943) 222
 phenolphthalein, (1941-2) 273
 gastra-intestinal disease, in, (1940) 544
 potassium iodide, leprosy, in, (1940) 381
 pregnancy, in diagnosis of, (1944) 23
 pregnitol, (1940) 478
 prothrombin, (1940) 386
 pulse response, (1941-2) 244
 respiratory function, (1943) 58
 Rorschach, (1940) 61, (1941-2) 85
 Schick, (1941-2) 209
 Schumm's, (1941-2) 170
 secretin, (1941-2) 322
 serum amylase, (1943) 296
 sodium lactate, intravenous dextrorotary, (1944) 287
 toluidine, (1940) 575
 tuberculin patch, (1940) 568, (1941-2) 292
 Vigotsky's, (1940) 60
 visual capacity of aviators, (1941-2) 30
 vitamin A absorption, (1941-2) 192
 Vollmer patch, (1940) 568
 Wassermann, (1940) 547 *See also* Wassermann reaction
 Weil-Felix, tick-bite fever, in, (1940) 85
 Wesselow and Griffiths, (1941-2) 206
 Widal, (1941-2) 63
 Woldman, (1941-2) 273
Tests
 absence of, (1941-2) 231
 bilharziasis of, (1941-2) 405
 biopsy of, (1939) 157
 male infertility, in, (1943) 352
 male sterility, in, (1941-2) 399, (1944) 380
 compensatory hypertrophy after unilateral orchidectomy, (1940) 550
 cord diseases, and, (1939) 559, (1940) 550-2; (1941-2) 405
 function, diathermy, effect of, (1940) 543
 gonadotrophic substance in, (1939) 158, 561
 pituitary implantation, (1939) 562
 infarction, (1940) 551
 spermatic cord, torsion of, (1943) 360
 tumours, (1939) 559, (1940) 551; (1941-2) 405
 chorionepithelioma, (1939) 559
 hydrocele,
 injection treatment, (1941-2) 406
 quinine dihydrochloride and urethane in, (1943) 360
 sclerotherapy, (1939) 560
 interstitial-celled, and precocity, (1941-2) 405
 seminoma,
 abdominal, (1941-2) 405
 teratoma, and, (1941-2) 405
 traumatic displacement causing, (1941-2) 405
 survival rates in malignant disease, (1939) 559
 X-ray therapy in, (1939) 560
 undescended, (1939) 561
 gonadotrophic substance in, (1940) 14, 551
 hormone treatment of, (1941-2) 5
 malignant disease in, (1943) 360
 treatment, (1941-2) 406
 chorionic gonadotrophic hormone and testosterone propionate, (1941-2) 406
 gonadotrophic hormone, (1941-2) 406
 surgical, (1940) 14, 551
 surgical and hormonal, (1941-2) 406

CUMULATIVE INDEX

- Testosterone, (1943) 96**
 blood pressure, effect on, (1941-2) 382
 carcinoma of breast, in, (1943) 164
 castrates, in, (1939) 535
 eunuchism and hypogonadism, in, (1941-2) 384, (1944) 49
 eunuchoidism, in, (1944) 50
 hepatic inactivation of, (1944) 369
 inunction in chronic mastitis, (1941-2) 175
 male breast hypertrophy, in, (1939) 261
 metrorrhagia, in, (1939) 431
 milk secretion, action on, (1939) 220
 propionate, (1943) 96
 action of, (1940) 132
 angina pectoris, in, (1943) 124, (1944) 140
 aplastic anaemia, in, (1939) 206
 bleeding, functional, in, (1944) 51
 climacteric, disorders, in, (1940) 248
 male, in, (1940) 249
 dysmenorrhoea, in, (1940) 282
 endometriosis, in, (1941-2) 221
 eunuchism and hypogonadism, in, (1941-2) 384
 female organism, response of, (1940) 524
 fractures, effect on healing of, (1940) 273
 gynaecological uses of, (1939) 35
 hyperaemia as test, (1940) 524
 hypogonadism, in, (1940) 525
 impotence, in, (1941-2) 261
 lactation, inhibition of, by, (1940) 500
 mastitis, in, (1940) 231
 menstruation, effect on, (1940) 526
 mental disorders, in, (1940) 525
 migraine, in, (1940) 409
 myotonia atrophica, in, (1940) 415
 oestrogenic property of, (1940) 524
 otosclerosis, in, (1944) 53
 prostatic enlargement, in, (1940) 483
 prostatic hypertrophy, in, (1941-2) 360
 puerperium, use in, (1940) 497
 sex organs of rats, effects of small doses on, (1941-2) 384
 undescended testis, in, (1941-2) 406
 uterine bleeding, in, (1940) 20, 526, (1941-2) 21
 vasomotor phenomena, (1940) 524
 women, biological effects in, (1940) 525
 prostatic enlargement treated with, (1944) 93
- Tetanus, (1939) 562, (1941-2) 406**
 abortion, induced, after, (1941-2) 126
 cephalic, injury of eye-ball, after, (1943) 361
 paralysis of facial nerve with, (1943) 361
 eye injury causing, (1944) 383
 immunity and immunization, (1940) 552, (1941-2) 407, (1943) 55, (1944) 383
 active, (1940) 552
 against diphtheria and, (1941-2) 260
 against enteric fever and, (1941-2) 407
 antitoxin, by, (1939) 562
 bovine, (1943) 361
 experimental in mice, with sulphonamides, (1939) 562
 sulphonamides in, (1940) 10
 toxoid in, (1940) 10, 137, (1941-2) 407
 anaphylaxis after, (1940) 552
 incidence of, (1940) 10
 trauma and, (1944) 383
 treatment, (1941-2) 407
 intracisternal injection of antitoxin, (1941-2) 407
 sedation, antitoxin, and hexamine, (1941-2) 407
 serum, (1940) 3, 10
 sulphapyridine and evipan sodium, (1941-2) 407
 sulphapyridine with hexobarbitone soluble, (1941-2) 118
- Tetany**
 adrenaline, effect of, (1944) 316
 cataract associated with, (1941-2) 186
 dihydrotachysterol in, (1940) 433
 infantile, vitamin D and, (1940) 130
 magnesium in, (1940) 114
 parathormone shock in, (1940) 433
- Tetany—continued**
 parathyroid glands and, (1944) 316
 psychosis complicating, (1941-2) 322
 post-operative, (1940) 433
- Tetrachlorethylene, ankylostomiasis, in treatment of, (1939) 219**
- Tetraethylthiuram monosulphide (T E T M.S.), scabies treated with, (1944) 117, 373**
- Thalamus, cortical activity, and, (1941-2) 89**
- Thallium acetate, epilation by, (1940) 328**
- Theca-celled tumour, ovary, of, (1940) 428; (1943) 294**
- Thecoma, ovary, of, (1944) 314**
- Theelin, gonorrhoea, in, (1939) 359**
- Theelin pellets, climacteric, in, (1940) 248**
- Theophylline**
 asthma, in, (1939) 200
 ethylenediamine, with (euphylline) *See also* Aminophylline
 asthma, in, (1943) 2
 heart disease, in, (1939) 20
 mono-ethanolamine, asthma, in, (1941-2) 158
- Therapeutics, advances in, (1941-2) 6**
- Thiamin**
 chloride in toxic amblyopia, (1939) 244
 deficiency, (1944) 204
 irritability due to, (1943) 64
 diabetes mellitus treated with, (1941-2) 422
 haemorrhage, effect in shock due to, (1943) 338
 hydrochloride *See* Vitamin B₁
 therapy, (1941-2) 422
- Thiazamide *See* Sulphathiazole**
- Thigh, amputation, ligature of femoral vein in, (1940) 395**
- Thio-bismol, control of malaria therapy, in, (1941-2) 301**
- Thiocyanates**
 dermatitis caused by, (1940) 257
 hypertension, in, (1943) 151
 psychosis caused by, (1943) 318
 toxic effects, (1941-2) 346
- Thiodiphenylamine, (1941-2) 122**
- Thioethamyl in labour, (1939) 397**
- Thomson's disease, quinine hydrochloride in, (1939) 166**
- Thoracic injury, (1941-2) 71**
 complications of, (1941-2) 75
 early surgery, importance of, (1941-2) 71
 operations, (1939) 26
 retained foreign bodies, (1941-2) 72
 special chest units, (1941-2) 71
 treatment, (1941-2) 72
- Thoracoplasty**
 pathology, (1943) 61
 pulmonary tuberculosis, in, (1940) 392
 results of, (1943) 61
 tuberculous-empyema, for, (1944) 220
- Thorax**
 lipoma, (1944) 295
 wounds, (1941-2) 71; (1943) 247, 249
 treatment, (1943) 311
- Thorek's operation, (1940) 306**
- Thorium dioxide, diagnosis of pyelephlebitis, in, (1941-2) 288**
- Thorotrast, arteriography, in, (1940) 103**
- Threadworms *See also* Oxyuriasis**
 appendicitis, causing, (1943) 129
 infestation, (1944) 308
 phenothiazine, in, (1941-2) 122, (1943) 287
- Throat**
 angina of, associated with mononucleosis, (1941-2) 235
 cancer, associated with epidermolycis bullosa, (1944) 225
 diseases of, (1941-2) 52
 larynx, (1943) 38
 sore, persistent myalgia following, (1943) 283
- Thrombi**
 ball, (1941-2) 252
 mural, as source of emboli, (1941-2) 218
- Thrombin**
 haemophilia, in, delayed formation of, (1940) 325
 rabbit as local haemostatic, (1943) 118

CUMULATIVE INDEX

- Thrombo-angiitis obliterans (Buerger's disease), (1939) 224
 aetiology, (1939) 224; (1943) 132
 prognosis, (1939) 225
 tobacco smoking and, (1941-2) 151
 treatment, (1943) 133
 alcohol injections, (1939) 225
 lumbar sympathectomy, (1939) 61
 oscillating bed, (1940) 194
 sodium tetrathionate and sodium thiosulphate, (1940) 194
- Thrombocytopenia, traumatic shock, in, (1941-2) 386
- Thrombocytopenic purpura
 aetiology, diagnosis, and treatment, (1941-2) 241
 parathyroid in, (1941-2) 241
 peripheral blood and bone marrow, reaction of, (1940) 327
 platelet-reducing extracts from spleen, (1940) 327
- Thrombokinae, (1940) 117, (1941-2) 163
- Thrombophlebitis
 acute superficial, treatment of, (1944) 401
 cavernous sinus, heparin and sulphonamide therapy, (1941-2) 408
 elastic adhesive bandages in, (1940) 582
 embolism, prevention of, (1940) 582
 erythraemia complicated by, (1941-2) 225
 heparin therapy, (1941-2) 296
 procaine hydrochloride injection, (1940) 583
 puerperal cerebral, (1943) 318
 pulmonary embolism and, (1941-2) 296
 operative treatment of, (1941-2) 296
- Thromboplastin, (1940) 117
- Thrombosis, (1939) 592. *See also* Vein diseases
 abdominal aorta, (1940) 195
 antithrombin in, (1943) 375
 axillary and subclavian veins, of, (1941-2) 420
 cavernous sinus, (1943) 14
 cerebral, (1940) 66
 carotid sinus stimulation causing, (1943) 129
 puerperium, in, (1943) 318
 cerebral veins, of, (1941-2) 92
 puerperal, (1941-2) 407
 coronary, (1940) 5. *See also* Coronary thrombosis
 dicoumarin as prophylactic, (1944) 322
 erythraemia complicated by, (1941-2) 225
 extremities, of, (1943) 134
 femoral, tick-bite fever, and, (1940) 84, 86
 heparin in, (1940) 137, 582, (1941-2) 335
 inferior vena cava, of, (1941-2) 420
 injected veins in excretion pycnography, in, (1941-2) 371
 intracranial venous, in puerperium, (1943) 4
 lateral sinus, treatment by sulphanilamide, (1943) 362
 meningeal (superficial cerebral) veins, (1940) 67
 mesenteric, (1941-2) 125
 novocain block in, (1943) 375
 obstetrics and gynaecology, in, (1944) 280
 post-operative, prevention, (1944) 322
 heparin in, (1941-2) 335
 septic, chemotherapy in, (1941-2) 59
 sinus, (1940) 66
 temporal artery, of, (1941-2) 152
 venous, central nervous system, in, (1940) 66, (1941-2) 92
 chemotherapy in, (1941-2) 59
- Thrush
 new-born, in, (1943) 218
 vaginal, (1941-2) 284
- Thymectomy, myasthenia gravis, in, (1943) 285
- Thymic death, (1944) 383
- Thymol
 actinomycosis, in, (1939) 186
 metacresyl acetate and, otomycosis treated with, (1940) 284
- Thymomas, (1943) 362
- Thymus gland, (1944) 47
 diseases, (1944) 383
 internal secretion of, (1944) 47
 lympho-epithelioma of, (1944) 383
 myasthenia gravis, and, (1940) 416
 enlargement, (1943) 284
 status thymico-lymphaticus, (1944) 383
- Thymus gland—*continued*
 tumours, (1944) 383
 myasthenia gravis, in, (1943) 283, 285, 362
 thymectomy, (1943) 285
 thymoma, (1943) 285, 362
- Thyroid gland, (1944) 46
 anaemia, relation to, (1939) 53
 angina pectoris and, (1940) 181
 bilateral exophthalmos in presence of sympathetic paralysis, (1940) 316
 diseases and tumours, (1939) 352; (1940) 314-7; (1941-2) 235. *See also* Goitre
 aberrant, lateral, (1943) 225
 malignant, (1940) 317
 adenocarcinoma, (1943) 224
 hyperthyroidism, and, (1943) 224
 adenoma, (1940) 314
 hippuric acid test, (1940) 317
 malignant, (1941-2) 236
 carcinoma, (1941-2) 236
 intranuclear inclusion bodies in, (1940) 241
 cystadenoma, malignant, (1940) 317
 hippuric acid test, (1940) 317
 iodine and, (1940) 314
 magnesium glutamate in, (1940) 317
 ovary, of, (1943) 294
 extract, bromine content of blood, reduction of, (1941-2) 337
 substitution therapy, (1943) 307
 galactose test, (1940) 316
 hypothalamus and, (1940) 66
 involution, (1944) 243
 mongolism, in, (1939) 432, (1940) 408
 pathology, (1940) 314, (1944) 243
 pituitary, relation to, (1940) 281
 pregnancy, in, (1940) 478
 senile changes, (1944) 243
 therapy, dysmenorrhoea, in, (1939) 321
 heart block resulting from, (1940) 315
 toxic effects, (1940) 315
- Thyroidectomy, (1940) 183, 338
 angina pectoris, in, (1939) 216
 diabetes insipidus, in, (1941-2) 205
 heart disease, for, (1939) 60
 subtotal, recurrence of hyperthyroidism after, (1943) 224
- Thyroidotrophic hormone, (1941-2) 382
- Thyrotoxicosis
 calcium and phosphorus metabolism in, (1941-2) 236, (1943) 223
 ergot alkaloids in treatment, (1941-2) 236
 myasthenia gravis associated with, (1943) 283
 pretibial myxoedema in, (1944) 307
- Thyroxine
 growth, relation to, (1940) 281
 periodic catatonia treated with, (1939) 119
- Tibia
 birth fracture of, bone-grafting in, (1940) 275
 fatigue fracture of, (1944) 206
 fractures, treatment of, (1943) 193
 pseudo-fracture of, (1940) 275
- Tibialis anterior muscle, hernia of, (1944) 305
- Tic douloureux, (1941-2) 314
- Tick-bite fever
 aetiology, (1940) 80
 agglutination, (1940) 85
 bacteriology, (1940) 81
 blood count, (1940) 85
 clinical picture, (1940) 82
 complications and sequelae, (1940) 84
 course and prognosis, (1940) 84
 definition, (1940) 80
 diagnosis, (1940) 84
 laboratory methods, (1940) 85
 fever, (1940) 84
 relapsing, (1943) 325
 geographical distribution, (1940) 80
 guinea-pigs, in, (1940) 82
 history, (1940) 80
 immunological reaction, (1940) 82
 incidence, (1940) 80
 incubation period, (1940) 83

CUMULATIVE INDEX

- Tick-bite fever—continued**
 lymphadenitis, (1940) 83
 mortality, (1940) 84
 paralysis, (1939) 241; (1944) 154
 parasites, (1940) 81
 pathology, (1940) 81
 primary lesion, (1940) 82
 prognosis, (1940) 84
 prophylaxis, (1940) 86
 rash, (1940) 84
 reservoir host, (1940) 81
Rickettsiae causing, (1940) 81
 symptoms, (1940) 82-4
 ticks transmitting, (1940) 81
 treatment, (1940) 86
 urine, (1940) 85
 vaccination, protective, (1940) 86
 vectors, (1940) 81
 Weil-Felix test in, (1940) 85
- Tick-typhus.** *See* Typhus fevers
- Tin, colloidal, typhoid fever treated with, (1944)**
 223
- Tinea**
 capitis, gentian violet treatment, (1940) 304
 mental deficiency associated with, (1939) 411
- Tinned foods, increased consumption of, (1940)** 4
- Tinnitus aurium, (1944)** 193
 meaning of, (1944) 195
 treatment by proslugin methylsulphate, (1941-2)
 201
 vascular origin of, (1941-2) 199
- Tissue culture, malignancy and, (1940)** 569
- Tobacco** *See also* Nicotine; Smoking
 chewing, and cancer of mouth, (1941-2) 308
 smoking, effect on alimentary tract of, (1939)
 551
- Tocopherol, (1940)** 131. *See also* Vitamin E
- Tocopherol acetate, (1943)** 96
- Toes, clubbing, hypertrophic osteoarthropathy and, (1944)** 276
- Toluene poisoning, (1943)** 364
- Toluidine test, haematuria, for, (1940)** 575
- Tomography, (1940)** 101
- Tongue**
 amputation, spontaneous, of, (1940) 411
 black hairy, (1940) 411; (1941-2) 308
 potassium chlorate therapy, (1940) 411
 radon therapy, (1940) 411
 carcinoma, in early life, (1940) 411
 chronic affections of the lung, in, (1941-2) 294
 diseases, (1940) 410
 leucoplakia, oestrogenic therapy, (1940) 410
- Tonsillectomy**
 bulbar poliomyelitis after, (1943) 362
 haemorrhages after, (1939) 564
 lung complications, (1939) 564
 nephritis, in,
 in children, (1940) 422
 prophylactic influence on, (1944) 309
 poliomyelitis and, (1941-2) 356, (1944) 39, 332
 prognosis after, (1939) 565
 respiratory infections, effects on, (1944) 168
 surrounding tissues, effects on, (1940) 553
- Tonsillitis**
 acute, chemotherapy in, (1941-2) 60
 brain abscess, sequel of, (1939) 254
 therapy, vitamin A, (1940) 128
 tuberculous, (1941-2) 408
- Tonsils**
 bacteriology, (1940) 553
 diseases, (1939) 563, (1940) 128, 553
 carcinoma, (1941-2) 349
 tuberculosis, (1939) 563; (1941-2) 408
 papilloma, (1939) 563
 vitamin C content of tonsils, (1939) 563
 enlarged, adenoids and, (1940) 553
 removal of. *See* Tonsillectomy
 streptococci, haemolytic, from, (1940) 553
- Torek's operation for undescended testis, (1940)**
 14
- Torsion**
 appendix epiploica, of, (1941-2) 125
 great omentum, of, (1941-2) 125
 spermatic cord, of, (1943) 360
- Torulin, (1940)** 128. *See also* Vitamin B₁
- Torulosis**
 central nervous system, of, (1944) 383
 cerebrospinal, (1944) 384
- Tourniquet**
 amputation, use in, (1943) 114
 new type of, (1940) 347
- Toxaemia hypothesis of cause of disease, (1939)**
 13
- Toxaemias of pregnancy, (1939)** 30. *See also* Preg-
 nancy, toxaeias of
- Toxicology, (1941-2)** 408; (1943) 6, 363. *See also*
 Poisoning
 homicidal, suicidal, and accidental, (1939) 565
 barbiturates, (1939) 568
 picrotoxin in treatment of, (1939) 569
 carbon monoxide,
 treatment of poisoning by, (1939) 566
 uraemia caused by, (1939) 565
 carbon tetrachloride, (1939) 570
 chenopodium oil, (1939) 569
 ethyl alcohol, (1939) 569
 mercury, acute poisoning, (1939) 568
 metacetaldehyde, (1939) 567
 nicotine, (1939) 567
 salicylates, (1939) 566
 stramonium, (1939) 567
 thallium sulphate, (1939) 568
 industrial poisoning, (1939) 570
 carbon tetrachloride, nephrosis caused by,
 (1939) 572
 cosmetic dermatitis, (1939) 572
 ethylene dichloride, (1939) 572
 fluorine, (1939) 571
 lead tetraethylbenzene (ethyl), (1939) 571
 phenol, (1939) 570
 phosphorus, (1939) 570
- Toxins, scarlet fever, for oral immunization against, (1941-2)** 378
- Toxoid**
 alum-precipitated, in diphtheria immunization,
 (1943) 55, 191
 diphtheria, (1941-2) 210
 formol, in treatment of leprosy, (1941-2) 284
 osteomyelitis, acute in, (1940) 226
 staphylococcus, prostatitis treated with, (1941-2)
 359
 tetanus, (1941-2) 407
 anaphylaxis after, (1940) 552
 immunization by, (1940) 10
 properties and dosage, (1940) 137
- Toxoplasma, acute disseminated encephalomyelitis
 due to, (1941-2)** 220
- Trachea**
 diseases, (1941-2) 412
 carcinoma, (1939) 573
 obstruction, leech cause of, (1939) 573
 sarcoma, (1940) 563
 tuberculosis, electrocautery in, (1939) 573
 inflammation, (1941-2) 412
- Tracheitis, helium-oxygen inhalation in, (1941-2)**
 281
- Tracheo-bronchial tuberculosis, (1943)** 62
- Tracheo-bronchitis, treatment by sulphonamides,
 (1941-2)** 412
- Tracheotomy, sudden death after, explanation and
 prophylaxis, (1939)** 398
- Trachoma, (1939)** 129, 573; (1940) 563-5
 aetiology, (1940) 564
 epidemiology, (1939) 573
 granules, (1940) 564
 inclusion bodies in, (1940) 564
 keratitis, recurrent ulcerative, in, (1940) 565
 Parinaud's oculo-glandular syndrome and, (1941-
 1942) 109
 treatment, (1940) 564
 sequelae, (1940) 565
 sulphapyridine, (1940) 564
 sulphonamides, (1939) 574, (1940) 564; (1941-
 1942) 412
 virus, (1940) 564
- Transfusion**
 intravenous, in shock (1941-2) 387
 using glass in haemorrhage, of, (1941-2) 269
- Transplantation**
 aponeurotic, head injury, in, (1940) 348

CUMULATIVE INDEX

- Transplantation—continued*
corneal, (1940) 254
ureters, of, (1940) 209
- Transposition of great vessels, (1941-2) 248
- Trasentin, (1939) 474
antispasmodic effect in gastro-intestinal disorders, (1940) 462
trasentin-6H, and, toxicity of, (1941-2) 347
- Trauma
coronary thrombosis due to, (1944) 140
epididymitis, acute, after, (1940) 291
epilepsy and, (1944) 226
hernia, relation to, (1940) 339
herpes, recurrent, due to, (1940) 341
myositis ossificans and, (1940) 413
osteoporosis caused by, (1941-2) 173
synovial granuloma, relation to, (1941-2) 274
tuberculosis and, (1940) 96
tumours, in relation to, (1941-2) 274
- Trench fever, (1939) 574
symptoms, (1944) 389
treatment, (1944) 389
- Trench foot, (1943) 1, (1944) 239
treatment, (1943) 217
- trophic disturbances resembling, (1940) 303
- Treponema pallidum* See *Spirochaeta pallida*
- Triazin arsenic, sleeping sickness treated by, (1943) 85
- Triazol See also Cardiazol
convulsion therapy, fatal cerebral fat embolism, (1941-2) 368
- Trichinella spiralis*, isolation of larvae from arterial blood, (1941-2) 413
- Trichiniasis, (1939) 575, (1941-2) 412
antigen sensitization, positive reactions after, (1944) 390
asymptomatic infection, (1943) 366
blood changes in, (1943) 366
cerebral symptoms, (1941-2) 90, (1943) 366
diagnosis and complications, (1939) 575
intra-dermal injection of antigen, (1944) 390
nervous symptoms complicating, (1944) 390
outbreak caused by sausages, (1943) 49, 366
outbreaks in England, (1941-2) 413
psychotic factors in, (1944) 390
treatment, (1939) 576
- Trichloroethanol, basal anaesthetic, as, (1939) 211
- Trichoeptitheloma, (1939) 539, (1941-2) 393
- Trichomonas vaginalis*
floraquin, treatment with, (1940) 382
infestation, (1941-2) 429
male genito-urinary tract, of, (1941-2) 417
leucorrhoea, in, (1940) 20
treatment, (1941-2) 429
vaginitis caused by, treatment by silver picrate, (1943) 379
vulvovaginitis caused by, (1944) 406
treatment, (1944) 406
- Trichophytosis, gentian violet and brilliant green in, (1940) 304
- Trichuriasis, iron and ammonium citrate in treatment, (1940) 420
- Tricresyl phosphate, poisoning by, (1941-2) 315
- Triethanolamine, dermatitis caused by, (1940) 258
- Trigeminal
neuralgia. See Neuralgia, trigeminal tract, division of pain fibres in neuralgia in, (1939) 446
- Trigonal muscle, (1944) 84
- Trinitrotoluene poisoning, porphyrinuria in, (1943) 6, 365
- Tri-ortho-cresyl phosphate
neuritis caused by, (1939) 13
poisoning by, (1944) 389
- Triphenylchloroethylene, action of, (1940) 523
- Triphenter minor, isolated rupture of, (1939) 235
- Tropical
diseases, (1943) 82; (1944) 390 See also Malaria; Plague; Typhus fever, Yellow fever
abou moukmouk, (1939) 576
chemotherapy in, (1941-2) 99; (1943) 85
drugs for, (1940) 136
general survey, (1939) 576
sulphonamides in, (1941-2) 344
- Tropical—continued*
medicine, (1939) 142; (1941-2) 96
advances in, (1940) 75; (1944) 96
hormones and vitamins in treatment, (1939) 149
kala-azar, (1939) 147
malaria, (1949) 142
relapsing fever, (1939) 147
trypanosomiasis and sleeping sickness, (1939) 145
typhus fevers, (1939) 147
yellow fever, (1939) 145
megalocytic anaemia, (1939) 204
differential diagnosis, (1939) 204
treatment, (1939) 204
ulcer, sulphonamide compounds in, (1940) 565
whale-oil application, (1941-2) 413
- Tropics
jaundice in, (1944) 276
rheumatic infection, acute, in, (1940) 510
- Trypanosomiasis, (1939) 576
antrypol in, (1940) 136
aromatic diamidines in, (1940) 136
chemotherapy in, (1940) 78
clinical picture, (1944) 99
congenital, (1944) 99
control and treatment of, (1939) 145
diamidines in, (1941-2) 100
germanin in prophylaxis, (1939) 576
suramin in, (1940) 136
synthalin in, (1940) 78
treatment, (1944) 100, 391
Bayer 205, (1943) 367
4 4'-diamidinostilbene, (1941-2) 413
triazin arsenic, (1943) 85
tryparsamide (1939) 146, (1940) 136
undecane diamidine, (1939) 577
visceral lesions, (1943) 367
- Trypanosomicides, (1940) 136
- Tryparsamide
neurosyphilis treated with, (1941-2) 316
nitritoid reactions and, (1940) 426
optic atrophy, in, (1941-2) 162
syphilitic primary optic atrophy, in, (1940) 210
toxicity, (1941-2) 317
trypanosomes, effect on, (1941-2) 332
trypanosomiasis, in, (1940) 136, (1944) 391
- Tsutsugamushi disease, (1940) 571
- Tubal pregnancy, (1939) 339, (1941-2) 228
aetiology, (1941-2) 228
differential diagnosis, (1941-2) 228
early recognition of, (1943) 207
pre-existing tubal infection, (1941-2) 228
- Tube
Miller-Abbot, (1940) 12; (1941-2) 272
Wangensteen, (1940) 12
- Tubercle
bacilli,
bactericidal effect of urea on, (1943) 308
staining with auramine, (1943) 368
endotoxoid,
Grasset's,
leprosy, in, (1941-2) 284
lupus vulgaris, in, (1941-2) 300
- Tuberculin
acne treated with, (1939) 186
Koch's old, in trigeminal neuralgia, (1939) 445
tests, (1940) 566
Mantoux and tuberculin patch tests, comparison of, (1940) 568
patch test, (1940) 94
pregnancy, during, (1940) 481
- Tuberculoid, leprosy, (1941-2) 283
- Tuberculoma, brain, of, (1940) 230
- Tuberculo-silicosis, X-ray findings in, (1941-2) 390
- Tuberculosis, (1939) 577, (1941-2) 414, (1944) 391-3
after-care, (1940) 96
age incidence, (1944) 392
anus, of, (1943) 128
articular symptoms, initial, (1940) 567
biliary tract, of, (1940) 305
blood viscosity, (1941-2) 414
bone, of, (1943) 160
insulin treatment, (1940) 226
bovine, infection in man, (1940) 97

CUMULATIVE INDEX

Tuberculosis—*continued*

carriers, unsuspected, (1941-2) 414
 childhood,
 death rate in, (1939) 39
 early, in, (1944) 392
 diagnosis, (1940) 567; (1941-2) 414; (1944) 393
 detection of tubercle bacilli with auramine dye,
 (1943) 368
 serial inoculation of sputum, (1944) 393
 tuberculin patch and Mantoux tests, (1940) 94,
 568
 Vollmer patch test, (1940) 568
 differential diagnosis,
 bacteriological, (1940) 567
 leprosy, (1943) 264
 epidemiology, (1940) 566, (1941-2) 414, (1944) 391
 erythema nodosum associated with, (1939) 336,
 (1941-2) 224
 experimental, effect of promin on, (1941-2) 336
 generalized, (1939) 582
 pulmonary and extra-pulmonary tuberculosis
 combined, (1939) 582
 simultaneous onset in identical twins, (1943) 368
 guinea-pig inoculation, (1939) 580
 hip, of, (1939) 391
 hypoproteinaemia in, (1943) 63
 immunity, (1939) 578
 allergy, and, (1941-2) 414, (1944) 392
 incidence of, (1941-2) 4
 age group, in, (1944) 392
 seasonal, (1940) 566
 infants, human form in, (1939) 577
 intestinal, (1941-2) 273
 calcium gluconate in, (1940) 355
 irido-cyclitis, (1941-2) 420
 joints, of, (1941-2) 274
 initial symptoms in, (1940) 567
 kidney, of, (1940) 365, (1944) 278
 knee, of, (1939) 391
 laryngeal, ionization in, (1939) 399
 life assurance and, (1940) 94
 localized lesions, treatment by promin, (1944)
 393
 mandible, of, (1940) 226
 Mantoux test, (1939) 579, (1940) 568
 mediastinum, of, (1941-2) 302
 Meinicke flocculation test, (1941-2) 414
 military, myeloid leukaemia and, (1940) 382
 morbid anatomy, (1944) 393
 nasopharynx, of, (1940) 390
 oxygen tension, effect of low, (1944) 392
 pancreas, of, (1940) 431
 patch test, (1940) 94
 pregnancy and, (1940) 95
 prevention, (1939) 580, (1941-2) 415
 primitive peoples, in, (1940) 95
 prognosis, (1940) 94, (1941-2) 414
 prostate, of, (1941-2) 359
 pulmonary, (1939) 411, (1941-2) 77
 adults, young, in, (1940) 566
 amenorrhoea, association with, (1940) 166
 anaesthesia, spinal, in, (1944) 136
 blood count in, (1944) 292
 bronchoscopy in, (1943) 62
 cavities,
 artificial pneumothorax treatment and, (1944)
 70
 healing of, (1944) 70
 inspissated, (1943) 269
 physics and pathology of, (1941-2) 77
 chemotherapy of, (1940) 6
 chronic, rehabilitation, (1944) 291
 classification, (1943) 61
 clinical picture, (1941-2) 291
 cor pulmonale, chronic, and, (1941-2) 291
 course and prognosis, (1941-2) 292; (1944) 291
 diabetes complicated by, (1939) 308
 diabetes mellitus associated with, (1941-2) 205
 zinc protamine insulin in, (1941-2) 206
 diagnosis, (1940) 6, 389
 radiological, (1940) 6
 diagnosis and differential diagnosis, (1941-2)
 292
 differential diagnosis, tuberculosis of naso-
 pharynx, (1940) 390

Tuberculosis—*continued*

pulmonary—*continued*
 eosinophilia in, (1941-2) 291
 epidemiology, (1944) 391
 erythrocyte sedimentation rate, (1944) 70
 extension after operations, (1941-2) 292
 gastric-intestinal complications, (1941-2) 292
 gastric lavage, (1940) 389; (1941-2) 292
 group surveys, (1940) 94
 heredity in, (1943) 62
 incidence, (1944) 391
 aged, in, (1944) 291
 army, in, (1943) 61
 Canadian Army recruits, in, (1944) 290
 mass radiography and, (1944) 68
 young adults, in, (1944) 291
 industry, in, (1943) 320
 Mantoux test, (1941-2) 292
 mass radiography, (1940) 6, 94, 103, 503, (1941-
 1942) 75, 292, (1943) 3, 319, 324;
 (1944) 68
 morbid anatomy and pathology, (1941-2) 291
 mortality, (1940) 566, (1941-2) 291
 pathogenesis, (1944) 70
 pituitary, atrophy, after, (1940) 531
 pleuritic effusion, eosinophilia in, (1941-2)
 291
 pneumolysis, extra-pleural, (1940) 95
 post-operative complication, (1941-2) 292
 pregnancy, in, (1940) 481
 problems of, (1940) 6
 prognosis, (1940) 94, (1944) 291
 sedimentation rate, clinical use of, (1944) 70
 prothrombin deficiency in, (1943) 230
 psychotic patients, in, (1940) 391
 recent work on, (1944) 70
 rehabilitation, (1944) 291
 screen photography, advantages of, (1941-2) 76
 sedimentation rate, (1944) 70, 159
 silicosis, relation to, (1944) 372
 social factors, (1941-2) 291
 sputum examination, (1941-2) 292
 survey of treatment, (1939) 114
 treatment, (1940) 390-4, (1941-2) 292; (1944)
 292
 apicolysis, paraffin-pack, (1940) 392
 ascorbic acid, (1940) 390
 cadmium sulphide, (1944) 292
 chemotherapy, (1943) 62
 collapse operations, partial, (1940) 392
 gold, (1944) 293
 hemi-diaphragmatic paralysis, (1941-2) 292
 high protein diet, (1944) 293
 insulin and high carbohydrate dietary, (1941-
 1942) 293
 intercostal nerves, temporary elimination of,
 (1940) 393
 paraffin pack, (1941-2) 293
 phrenic paralysis, (1941-2) 292
 pneumolysis, (1940) 95, 393
 pneumoperitoneum, (1943) 269
 pneumothorax,
 ambulatory, (1944) 292
 artificial, (1940) 390; (1941-2) 293, (1944)
 70
 promin, (1943) 62
 social administration and colonization, (1941-
 1942) 292
 sulphanilamide, (1940) 390
 sulphapyridine, (1940) 390
 surgical, (1940) 392-4
 thoracoplasty, (1940) 392
 vitamin K in haemoptysis, (1943) 63
 tuberculin patch test, (1941-2) 292
 tuberculin tests and, (1940) 566
 uterine tuberculosis associated with, (1941-2) 22
 X-ray examination, (1941-2) 292; (1943) 319-
 321, 324
 recent work on, (1940) 94-7
 red-haired persons, susceptibility of, (1941-2)
 414
 renal. *See* Kidney, tuberculosis
 skin, of, (1939) 538
 social hygiene, (1940) 96
 spine, of, (1939) 544; (1941-2) 396

CUMULATIVE INDEX

Tuberculosis—continued

- spleen, of, (1940) 541
 - splenomegaly, (1940) 541
 - sputum, serial inoculation, (1944) 393
 - stomach, of, anaemia, pernicious, associated with, (1940) 169
 - sulphonamide compounds in, (1940) 95, 568
 - teeth as indicators of, (1939) 579
 - tonsils, of, (1939) 563; (1941-2) 408
 - trachea, of, (1939) 573
 - tracheo-bronchial, (1943) 62
 - trauma and, (1940) 96
 - treatment, (1941-2) 415
 - antituberculosis endotoxoid, (1939) 581
 - cod-liver oil, (1941-2) 415
 - local lesions, various, of, (1941-2) 415
 - promin, (1944) 393
 - sulphapyridine, (1941-2) 415
 - sulphonamide compounds, (1940) 95, 568
 - surgical, rubrophen in, (1939) 581
 - vitamin C, (1941-2) 415
 - tuberculin ointment test, (1939) 579
 - tuberculin patch test, (1939) 578, (1940) 568
 - urinary, (1940) 365
 - urogenital, (1944) 278
 - uterus, of, (1939) 588
 - vaccination, multiple puncture, (1939) 580
 - vitamin A deficiency, (1939) 577
 - Vollmer patch test, (1940) 568
 - war and, (1940) 96, (1944) 9
- ## Tuberculous
- ankle, (1941-2) 274
 - duodenal ulcer, perforation of, (1941-2) 326
 - emphysema, obstructive, in children, (1941-2) 219
 - empyema *See* Empyema
 - gastritis, experimental, (1944) 242
 - infections, promin in treatment, (1941-2) 119
 - kerato-iritis, beta-rays of radium in, (1940) 579
 - meningitis *See* Meningitis
 - pleuritic effusion, (1941-2) 291
 - tarsus, (1941-2) 274
 - tonsillitis, (1941-2) 408
 - ulceration, in gastro-intestinal tract, (1941-2) 273
 - ulcers of stomach, (1941-2) 401
- ## Tuberous sclerosis *See also* Epiloia
- eye lesions in, (1943) 204
 - hamartial nature of, (1943) 204
 - phakomas in, (1943) 204
- ## Tularaemia, (1939) 582
- agglutination reactions, (1943) 369
 - bacteriology and morbid anatomy, (1941-2) 415
 - causal organism, culture of, (1943) 368
 - clinical picture, (1939) 582
 - diagnosis, (1939) 582
 - meningitis, from, (1941-2) 415
 - intracellular parasitism, (1941-2) 415
 - pulmonary, (1943) 369
 - sulphanilamide in, (1940) 569
 - malignant, diagnosis by sternal puncture, (1940) 569
 - oestradiol producing, (1940) 527
 - progesterone as anti-tumourigenic agent, (1940) 527
 - sternal puncture in diagnosis, (1940) 569
 - stilboestrol producing, (1940) 521
 - tissue culture, (1940) 569
 - treatment,
 - miscellaneous methods, (1943) 369
 - sulphonamides, (1943) 369
- ## Tulle gras dressings, (1941-2) 263
- ## Tumours, (1939) 583; (1943) 370. *See also* Carcinoma
- fibroid, uterine, (1939) 588
 - gastric, (1939) 549
 - giant-celled, of bone, (1941-2) 172
 - glomus, (1943) 345
 - lung, of, (1939) 415
 - lymphatic glands, of, (1939) 420
 - malignancy,
 - diagnosis of, (1939) 583
 - gradation of, (1943) 370
 - mitosis,
 - coefficient, (1939) 583
 - effect of irradiation on, (1941-2) 416

Tumours—continued

- multinucleosis among Bantus, (1941-2) 416
 - oestrogen and androgen on cancer tissue, effects of, (1941-2) 183
 - organotherapy, (1939) 583
 - radio-sensitivity of, (1941-2) 372
 - renal, (1939) 393
 - 'serum-boiling' test, (1939) 583
 - uniovular and binovular twins, in, (1941-2) 254
 - urethra, of (melanoma), (1939) 585
- ## Turner's syndrome, (1943) 197
- ## Twins
- carcinoma of large intestine in, (1939) 288
 - Hodgkin's disease in, (1943) 243
 - identical,
 - coeliac disease in, (1941-2) 191
 - generalized tuberculosis in, (1943) 368
 - macrogenitosomia in one twin, (1940) 152
 - non-identical, diabetes insipidus in, (1943) 185
 - tumours in uniovular and binovular, (1941-2) 254
- ## Tympanic membrane
- blast, injuries due to, (1940) 47
 - 'blue drum' or idiopathic haemo-tympanum, (1943) 198
 - explosions, effect of, (1940) 47
 - rupture, (1940) 46
- ## Typhoid bacillus. *See* *Bacterium typhosum*
- ## Typhoid fever
- aetiology, (1944) 222
 - carriers of, (1940) 289
 - type D4 carrier, (1944) 223
 - confusional states, adrenal cortical extract in, (1940) 290
 - diagnosis and differential diagnosis, (1940) 290
 - faeces, isolation of bacteria from, (1940) 290
 - H antigen, pre-operative injection of, in cataract (1940) 243
 - nutrition in, (1941-2) 221
 - prophylaxis, (1940) 290
 - psychoses complicating, adrenal cortical extract in, (1940) 290
 - sulphapyridine, (1940) 290
 - treatment, (1944) 223
 - bananas, (1941-2) 221
 - colloidal tin, (1944) 223
 - mandelic acid, (1943) 202
 - sulphaguandine, (1941-2) 222, (1944) 223
 - 'typhoid Mary', (1940) 289
 - urine, isolation of bacteria from, (1940) 290
 - Vi bacteriophage, use of, (1944) 222
- ## Typhus fever, (1941-2) 98, (1943) 4, 84, 370 *See also*
- ## Typhus fevers
- diagnosis, (1943) 84
 - epidemic or louse-borne,
 - clinical picture and course, (1944) 394
 - Mexican murine vaccination, (1941-2) 416
 - prison camp observations in, (1944) 394
 - epidemiology, (1944) 98
 - exanthematous and endemic, cross-immunity between, (1943) 371
 - lice, control of, (1943) 85
 - non-epidemic or epizootic, (1944) 395
 - present war, during, (1944) 11
 - tick-typhus,
 - toxaemic signs in guinea-pigs, (1944) 395
 - treatment, (1943) 84, (1944) 99
 - Cox vaccine in, (1943) 56, 84
 - immunization against, (1943) 56
 - murine infection, by, (1943) 371
- ## Typhus fevers, (1939) 583; (1940) 4, 76, 570; (1944) 394. *See also* Typhus fever
- antigen types, (1944) 394
 - blood changes in, (1940) 570
 - cerebrospinal fluid in, (1940) 571
 - classification, (1944) 394
 - epidemic, (1940) 76
 - epidemiology, (1940) 570
 - mute-typhus, (1940) 571
 - murine typhus, vaccine, (1940) 571
 - prophylaxis, (1940) 76-8, 571
 - Rickettsiae* vaccines in, (1940) 76-8
 - South Africa, in, (1939) 583
 - Tsutsugamushi*, (1940) 571
 - vaccines in, (1939) 147; (1940) 76-8

CUMULATIVE INDEX

Tyrosin, (1944) 116
derivatives, (1943) 308

U

Ulceration

caecum, colon, and rectum, of, simple, (1941-2) 193
chronic undermining, (1940) 571
zinc peroxide in, (1940) 572
sulphanilamide, and, (1940) 572
corneal, (1940) 253, (1944) 192
cyclical buccal and genital, (1943) 20
gastro-jejunal, (1941-2) 328
jaws, of, non-malignant, (1941-2) 308
leg, of, skin-grafting in, (1944) 395
lepromatous, (1941-2) 284
phagedenic, (1941-2) 392
pharynx, of, decubital, (1941-2) 350
radioneurotic, zinc treatment, (1941-2) 372
rodent. *See* Rodent ulcer
streptococcal, sulphanilamide in, (1940) 571
tropical, whale-oil application in, (1941-2) 413
tuberculous,
duodenum, of, (1941-2) 326
gastro-intestinal tract, of, (1941-2) 273
stomach, of, (1941-2) 401
varicose, treatment of, (1944) 401

Ulcerative colitis *See* Colitis, ulcerative
Ulceron

cerebrospinal fever, in, (1939) 275
chancroid, in, (1939) 277
chemistry and pharmacology of, (1939) 170
gonorrhoea, in, (1939) 357
impetigo, in, (1939) 381
ophthalmia, epidemic gonorrhoeal, in, (1943) 178
osteomyelitis, in, (1939) 254

Ulna, fracture of, dislocation of head of radius associated with, (1940) 276

Ultra-violet irradiation

air, of, (1940) 150, (1944) 42, 63
hospitals, in, (1940) 150, (1941-2) 130
bactericidal power of, (1939) 187, (1943) 53, 105
carcinogenic action, (1940) 151, (1941-2) 129
colds, for, (1939) 284
dangers, (1940) 151
disinfection by, (1944) 42
erythema caused by, (1940) 151
hidradenitis suppurativa, in, (1939) 320
immunity, effect on, (1941-2) 260
operating rooms, in, (1940) 150
post-irradiation necrosis, in, (1941-2) 130
respiratory infections, prevention of, (1940) 150
surgery, in, (1940) 150
tanning, delayed, brought out by blood transfusion and, (1940) 151
toxic goitre, in, (1939) 354
whooping-cough, in, (1940) 595
wounds, of, (1940) 150

Umbilical cord

hernia in, (1941-2) 255
prolapse of, (1941-2) 278

Umbilicus

diphtheria of, (1940) 572
endometriosis of, (1939) 329
fistula, (1943) 371

Undescended testis, malignant disease in, (1943) 360

Undulant fever, (1939) 584, (1941-2) 416, (1944) 395. *See also* Abortus fever

cows and pigs as source of infection, (1944) 395
milk, raw, causing, (1940) 143
Nigeria, in, (1943) 371
serum-agglutinin test, (1940) 573
stibophen in, (1940) 136
sulphonamides in, (1939) 584, (1940) 143, 573; (1941-2) 100
vaccine and sulphonamide therapy, (1940) 573
vertebral lesions, (1940) 573

Uraemia, (1944) 396

acute, polycystic disease of kidneys causing, (1941-2) 275
aetiology, (1944) 396
E.M.S. II

Uraemia—continued

desoxycorticosterone acetate, in, (1941-2) 417
gastric haemorrhage and blood transfusion, after, (1943) 372
heart in, (1944) 396
histological changes, (1944) 396
pre-operative treatment with magnesium sulphate, (1943) 372
X-ray therapy of leukaemia causing, (1940) 384

Urea

bactericidal effect on tubercle bacilli, (1943) 308
caroid, and, in chronic otitis media, (1939) 324
clearance test, Peters and van Slyke, (1940) 118
dermatitis gangrenosa infantum treated with, (1939) 300
mercurial diuretics, and, in cardiac dropsy, (1940) 377
warts treated with, (1940) 533

Ureides, cyclic, poisoning by, (1940) 557

Ureter

accidental bilateral ligation of, (1941-2) 276
blockage, bilateral, following sulphonamide therapy, (1940) 369
calculus, (1940) 369 *See also* Calculus, ureteral carcinoma,
clinical picture, (1941-2) 277
metastatic, (1941-2) 278, 361
nephro-ureterectomy for, (1941-2) 277
surgical injuries, (1941-2) 418

dilatation,

hormones producing, (1943) 19
stasis, in, (1943) 152
injury, (1943) 258
strictures, relation to hypertension, (1943) 152
transplantation of, (1940) 14, 209
tumour, primary benign, (1943) 258
Ureterocele, (1941-2) 231, (1943) 257

Urethane

hydrocele treated by quinine dihydrochloride and, (1943) 360
quinine and, (1941-2) 112

Urethra

abnormalities, (1940) 576
obstruction, danger of infection in, (1941-2) 418
diseases, (1939) 584, (1940) 574, (1941-2) 417
carcinoma, incidence and treatment in male and female, (1940) 575, (1943) 373
enuresis, treated by dilatation, (1943) 202
melanoma, (1939) 585
mycotic urethritis, (1939) 585
urethritis, sulphanilamide in, (1939) 584
female,
congenital stricture, (1941-2) 418
injury, (1944) 397
stress incontinence, (1944) 397

male,

anomalies, (1941-2) 417
inflammations, (1941-2) 417
meatal stenosis, (1940) 574
rupture, (1943) 372
surgical treatment, (1944) 397
Trichomonas vaginalis infestation, (1941-2) 417
verumontanum, hypertrophied, (1940) 574
congenital, (1941-2) 417
urinary extravasation from, (1943) 373

Urethritis

follicularis, (1940) 574
neoparsphenamine treatment, (1941-2) 417

Urinary

amylase, (1940) 575
antiseptics, sulphonamides as, (1940) 457
antiseptics, sulphonamides as, (1941-2) 117
tract,
anomalies, in relation to chronic pyuria, (1941-2) 231
carcinoma of cervix, effect of, (1940) 578
complications due to sulphonamides, (1941-2) 346
infection,
congenital obstruction and, (1941-2) 418
sulphanilamide in, (1940) 208, (1941-2) 344

CUMULATIVE INDEX

Urinary—*continued*
 tract—*continued*
 infection—*continued*
 sulphathiazole in, (1941–2) 344
 sulphonamide compounds in, (1943) 72, 307
 urogram, delayed, (1940) 370

Urine
 alcohol in, estimation of, (1941–2) 134
 amylase estimation, (1940) 575
 androgenic activity of, (1944) 48
 anterior pituitary hormone in, (1944) 397
 blood in, (1940) 575
 examination, (1939) 585; (1940) 575, (1941–2) 418, (1944) 397
 bacteriology, (1939) 585
 excretion, Addison's disease, in, (1943) 106
 extravasation of, (1943) 373
 hormonal influences on, during pregnancy, (1944) 23
 incontinence, stress, (1944) 397
 lead, detection of, (1944) 397
 lead excretion in, (1939) 400
 nicotine, excretion of, (1944) 324
 nicotinic acid in, (1940) 115
 oestradiol benzoate, effect on output, (1940) 522
 oestrogenic activity of, (1944) 49
 pH, and bactericidal power of sulphanilamide, (1940) 459
 pregnanediol in, (1941–2) 357
 prior to and after foot-racing, (1939) 235
 protein fractions, examination of, (1944) 397
 proteins of, (1940) 121
 retention, post-operative, bacteriology of, (1940) 208
 spinal anaesthesia, after, (1941–2) 162
 treatment by β -methylcholine urethane, (1941–1942) 161
 stasis, relation to hypertension, (1943) 152
 sulphonamides in, bacteriostatic and germicidal effect of, (1940) 457
 suppression, post-partum, (1940) 499
 tubercle bacilli in, (1940) 365, (1944) 278
 vitamin B₁ in, (1940) 115

Urobilin, excretion, and blood destruction, (1944) 303

Urogastone, peptic ulcer treated with, (1943) 301

Urogenital diseases
 non-venereal, (1939) 157
 dyscyesis, (1939) 158
 male sterility,
 sub-fertility, gonadotrophic hormone treatment in, (1939) 157
 testicular biopsy in, (1939) 157
 sterilization, (1939) 158
 pyelitis, (1939) 159
 venereal, (1939) 150
 gonorrhoea, (1939) 155
 lymphogranuloma inguinale and Waelch urethritis, (1939) 155
 preventive measures, (1939) 150
 soft chancre, granuloma venereum and gangrenous balanitis, (1939) 155
 syphilis, (1939) 151

Urogenital organs
 abnormalities, (1939) 586, (1940) 576, (1941–2) 418
 penis, congenital absence of, (1939) 586
 ureterocele, (1939) 586

Urogram, delayed, (1940) 370

Urography
 excretion, (1941–2) 372
 renal, (1944) 357

Uropac, iodoxyl, official name for, (1940) 127

Uroselectan B
 excretion pyelography, in, (1941–2) 371
 induction of labour by, (1941–2) 19
 iodoxyl, official name for, (1940) 127
 thrombosis of injected veins, (1941–2) 371

Urticaria, (1939) 200
 acanthosis nigricans associated with, (1944) 120
 alkaline diet and sodium bicarbonate, (1939) 201
 autochaemotherapy, (1939) 200
 histaminase, in, (1940) 163

Urticaria—*continued*
 insulin,
 causing, (1940) 160
 shock in, (1939) 201
 multiformis endemica, (1940) 464
 pathogenesis, (1944) 126
 survey of causes of, (1939) 64

Utsils, cadmium plated, poisoning due to, (1943) 6, 364

Uterine
 inertia, oestrogenic hormones in treatment of, (1939) 31
 muscle, effect of raspberry-leaf extract on, (1941–1942) 20

Utero-placental apoplexy, (1944) 24

Uterus
 absence, hereditary, (1940) 577
 adeno-acanthoma of corpus, (1940) 578
 adenoma, hyaline, of cervix, (1940) 577
 adenomyoma, (1940) 288
 carcinoma,
 cobra veni for relief of pain, (1941–2) 419
 corpus uteri, of, (1940) 578
 Fallopian tubes, secondary growth in, (1941–2) 228
 carcinoma, cervix, (1939) 588, (1940) 578
 acetone as haemostatic, (1939) 589
 endometriosis associated with, (1941–2) 419
 glandular changes, (1939) 588
 local refrigeration in, (1941–2) 419
 occurring before the age of twenty, (1940) 578
 pregnancy, complicating, (1939) 589
 radium,
 interstitial, (1940) 578
 X-ray therapy, and, (1940) 504, (1941–2) 419
 urinary tract, effect on, (1940) 578
 X-ray therapy, (1939) 589

contractions,
 dysmenorrhoea, and, (1941–2) 214
 mechanical recording of, (1944) 352
 stilboestrol, effect of, (1940) 372

corpus uteri, adeno-acanthoma, (1940) 578

developmental abnormalities, (1939) 587
 underdeveloped uterus, gonadotrophic hormone therapy for, (1939) 487

diagnosis, general, (1939) 587
 biopsy of uterine mucosa, (1939) 587
 diseases and disorders, (1940) 577–9, (1941–2) 419
 endometrial mole-type tumours, (1940) 577

fibroids,
 incidence in white women and negroes, (1944) 398
 treatment,
 myomectomy, (1944) 27
 surgical, (1939) 588

fibromyoma,
 experimental production, (1944) 27
 irradiational treatment, (1941–2) 419
 oestrogen injections, prevention after, (1941–2) 383
 oestrogens producing, (1944) 27

haemangioma, X-ray therapy, (1941–2) 419

haemorrhage,
 functional, stilboestrol in, (1944) 26
 investigation of, (1944) 302
 oestrogens in, (1941–2) 21
 pregnanediol excretion, (1940) 21
 testosterone propionate in, (1940) 20; (1941–2) 21

hydatid cyst, (1941–2) 419

inversion, puerperal, (1940) 373, 498; (1944) 280

leiomyomas, mitotic activity in, (1944) 398

lymphangio-endothelioma, potential malignancy, (1943) 373

mesodermal tumours, mixed, (1940) 577

metastatic carcinoma of, (1943) 373

oestrogen, prolonged administration, effect of, (1940) 521

physiology, (1939) 586
 motility, (1939) 586

posterior pituitary extract,
 effect of, (1940) 453
 post-partum, response to, (1940) 498

post-partum,
 effect of ergot in promoting involution, (1944) 23
 effect of stilboestrol on, (1941–2) 370

CUMULATIVE INDEX

Uterus—continued

- rupture of, during labour, (1944) 279
- tuberculosis, (1939) 588
- endometrium, of, (1939) 588
- pulmonary tuberculosis associated with, (1941–1942) 22
- tumours, (1939) 588; (1940) 577–9; (1941–2) 419
- Uveal tract
- diseases, (1939) 590; (1940) 579; (1941–2) 420
- angioid streaks, (1939) 590
- ciliary neuralgia, (1939) 590
- inflammation, (1941–2) 420
- melanoma, (1943) 374
- sarcoma, prognosis of, (1941–2) 420
- Uveo-parotitis, (1941–2) 420

V

Vaccination

- convalescent serum, effect of, (1940) 579
- encephalo-mylitis complicating, (1939) 328, (1943) 201
- generalization, (1944) 399
- influenza, in, (1943) 5
- Rivers's culture virus and calf lymph virus, (1940) 579
- yellow fever and smallpox, (1940) 596
- Vaccine
- colds, for, (1939) 284; (1941–2) 193
- spray, intranasal, (1941–2) 193
- dermatophytosis treated with, (1939) 343
- enteric fevers, in, (1941–2) 261; (1944) 222
- general paralysis of insane, in, (1941–2) 315
- influenza treated with, (1944) 264
- meningitis, in, (1939) 427
- Mexican murine typhus, in, (1941–2) 416
- prophylactic, (1940) 4
- shock reactions due to, (1939) 379
- T.A.B.,
 - epidemic myositis following, (1943) 282
 - general paralysis of insane, in, (1939) 448
 - herpes labialis caused by, (1943) 242
- T.A.B.C., (1941–2) 261
- therapy, decline of, (1940) 4
- typhus fevers, in, (1939) 147, (1940) 76–8, 571; (1941–2) 416, (1943) 84
- ulcerative colitis, in, (1939) 288
- undulant fever treated with neoprontosil and, (1940) 573
- whooping-cough, in, (1943) 380
- Vaccinia
- generalized, (1944) 398
- positive syphilitic reactions in, (1943) 88
- vaccination, and, (1939) 590
- subcutaneous vaccination of adults, (1939) 590
- Vaccinola, (1944) 398
- Vagina
- absence, congenital, (1944) 234
- acidulation of, in vulvovaginitis, (1940) 320
- carcinoma, radium therapy, (1944) 358
- cleanser, effective, (1940) 593
- cysts and tumours, (1941–2) 430
- dermoid, obstructing labour, (1940) 373
- diphtheria, (1941–2) 429
- diseases, (1941–2) 429; (1944) 405
- fistulae, (1941–2) 430
- hydrogen-ion concentration, (1940) 22
- hydrometocolpos in infants, (1941–2) 430
- mesodermal tumours, mixed, (1940) 577
- moniliasis of, (1941–2) 284; (1943) 379
- mycotic infections during pregnancy, (1940) 594
- posterior fornix, needle puncture of, (1940) 23
- Trichomonas vaginalis* infestation, (1941–2) 429
- trichomoniasis, (1944) 406
- treatment, (1944) 406
- vesico-vaginal fistulae, operation for, (1941–2) 430
- Vaginal
- discharges, floraquin, in, (1940) 382
- smear,
 - incomplete abortion, and, (1940) 141
- ovulation, during, (1944) 26
- thrush, (1941–2) 284

Vaginitis

- bismuth therapy causing, (1940) 550
- chrysotherapy causing, (1944) 405
- diphtheritic, (1941–2) 429
- gonococcal, oestrogenic therapy, (1940) 594
- monilial, and leucorrhoea, (1941–2) 284
- post-menopausal, treatment, (1941–2) 429
- senile, treatment of, (1941–2) 429; (1944) 27
- synthetic oestrogens in, (1939) 35
- silver picrate, in, (1943) 379
- stilboestrol in, (1940) 132
- Trichomonas vaginalis* causing, (1941–2) 429; (1943) 379
- triphenylchloroethylene in, (1940) 523
- Valley fever, (1943) 146, 205. *See also* Coccidioidomycosis
- coccidioidal granuloma and, (1944) 157
- Valve amplifiers for the deaf, (1939) 101
- Valvulae conniventes, (1941–2) 27
- Vanadium, poisoning by, (1940) 562
- Van den Bergh reaction, diabetes mellitus, in, (1940) 263
- Vaporizers, Oxford anaesthetic, (1944) 137
- Varicella. *See* Smallpox
- Varicose ulcer
- histamine iontophoresis, (1940) 581
- treatment with blood or plasma, (1944) 401
- vitamin B₁ therapy, (1940) 581
- Varicose veins, (1944) 399–403
- aetiology, (1940) 580
- circulatory efficiency and, (1944) 399
- Forces, in, (1944) 400
- oesophageal, sodium morrhuate in, (1940) 428
- recent work on, (1944) 401–3
- recurrence, factors in, (1940) 581
- retina in diabetic retinitis, of, (1941–2) 376
- saphenous vein, internal, removal of, (1940) 13
- sensitivity to sodium morrhuate and monoethanolamine oleate, (1941–2) 421
- significance of small intracutaneous veins on chest, (1941–2) 421
- thrombophlebitis, acute superficial, and, (1944) 401
- treatment,
 - according to site of lesions, (1943) 374
 - injection, (1940) 13, 580, (1944) 400
 - sodium ricinoleate and heparin, (1944) 399
 - operative, (1940) 13, 428, 581, (1944) 400
 - sclerosing solutions, (1943) 374
 - sodium morrhuate, in, (1940) 428, 581
 - ulceration, treatment of, (1944) 401
- Vascular
- anastomosis, soluble rod method of, (1941–2) 264
- changes, associated with splenic disease, (1941–2) 397
- disease, obliterated, sympathectomy for, (1943) 134
- peripheral,
 - action of vasodilator drugs, (1941–2) 151
 - plethysmographic method of measuring blood flow in, (1941–2) 151
- disturbance
 - peripheral, (1940) 196, 452; (1944) 81
- Vaseline, toxic dermatitis caused by, (1939) 299
- Vasoconstriction, (1944) 81
- Vasoconstrictor, shock treated by transfusion and, (1941–2) 388
- Vasodilatation, reflex, (1944) 81
- Vasodilators, action in peripheral vascular diseases, (1941–2) 151
- Vasomotor rhinitis, (1940) 162. *See also* Rhinitis, vasomotor
- Vasospasm, peripheral, tobacco smoking causing, (1940) 557
- Vein
- diseases, (1939) 591; (1940) 580–3; (1941–2) 420; (1943) 374; (1944) 399–403
- thrombophlebitis, (1939) 592
- mecholyt iontophoresis treatment, (1939) 592
- post-operative, (1939) 592
- sleep therapy, after, (1939) 592
- thrombosis, (1939) 592
- axillary and subclavian veins, of, (1939) 593
- multiple thromboses, (1939) 592
- post-operative, prevention of, (1939) 593

CUMULATIVE INDEX

- Vein**—*continued*
diseases—*continued*
varicose veins, (1939) 591. *See also* Varicose veins
allergic manifestations following injection treatment, (1939) 591
ulceration, treatment of, (1939) 591
obstruction, (1941-2) 420
tumours, (1941-2) 422
vertebral, (1941-2) 89
wounds, of, (1941-2) 421
Veldt-sore, incidence among fair-haired persons, (1944) 403
Vena cava, inferior
leiomyosarcoma of, (1941-2) 422
thrombosis of, (1941-2) 420
Vena cordis magna, ligation of, (1943) 124
Venereal diseases, (1941-2) 102, (1943) 87. *See also* Gonorrhoea, Syphilis
civil practice and Forces, in, (1944) 102
compulsory treatment, (1944) 102
incidence, (1941-2) 102, (1943) 87, (1944) 102
prevention and treatment, (1940) 87, (1941-2) 102, (1944) 244
pirophylaxis by colloidal silver and mercury ointment, (1940) 450
recent work on, (1944) 102
war and, (1940) 87, (1944) 10
Venom
cobra, for relief of pain due to cancer, (1941-2) 184
snake, application in various diseases, (1943) 303
Venous
occlusion, effect on arterial flow to extremity, (1941-2) 151
retardation, developmental, (1943) 293
thrill, abdominal in cirrhosis of liver, (1941-2) 288
thrombosis,
central nervous system, in, (1941-2) 92
intracranial, (1943) 4
Ventricular
fibrillation, mechanism of, (1941-2) 150
septum, transposition of great vessels with defects of, (1941-2) 248
Ventriculography, (1940) 102, (1944) 165
diagnosis of cerebral tumour, in, (1941-2) 175
Veratrum viride therapy in eclampsia, (1941-2) 358
Veritol, (1939) 164
blood pressure, effect on, (1940) 463
Vertebra
fifth lumbar, sacralization of, (1940) 207
fourth lumbar, spondylolisthesis of, (1941-2) 161
convulsion therapy causing, (1941-2) 80
fracture, convulsion therapy causing, (1940) 491
osteomalacia, (1940) 540
plana, (1940) 539
undulant fever, lesions in, (1940) 573
Vertebral column. *See* Spine
Vertigo, (1939) 593, (1943) 38, 376
aetiology, (1943) 38
alcohol, injection of, in treatment, (1939) 594
aural, treatment of, (1939) 88
aural, or labyrinthine, (1941-2) 422, (1944) 404
labyrinthectomy, (1940) 583
Portmann's operation, (1940) 583
clinical picture, (1940) 583
Eustachian tube obstruction causing, (1943) 376
Ménière's syndrome, (1939) 593
treatment,
alcohol injection of labyrinth, (1943) 39, 376
eighth nerve, division of, (1943) 38
histamine, (1943) 39, 377
sodium-free diet, (1943) 39, 377
Verumontanum, hypertrophy of, (1940) 574
congenital, (1941-2) 417
Vesical
bilharziasis, treatment of, (1943) 143
neuralgia, (1940) 207
Vesicant gases, effect of liquid mustard-gas on eyes, (1940) 311
Vesicovaginal fistula, operation for, (1941-2) 430
Vestibular function, (1944) 88
Vibration sense, (1939) 256
myotonia atrophica cause of disturbance of, (1939) 438
Vibrio septique, M & B 693, effect of, (1940) 134
Vigotovsky's test, (1940) 60
Vincent's angina, (1943) 2
iodine potassium and iodide in, (1940) 410
leukaemia, aleukaemic, and, (1940) 383
nicotinic acid in, (1940) 410
pharyngitis, acute, and, (1941-2) 349
Vinyl ether (vinesthene) anaesthesia, (1939) 208
convulsions, (1940) 175
Vioform, vaginitis, in, (1939) 600
Virilism
adrenal, (1943) 108
renal hypernephroma and, (1941-2) 133
women, in, (1944) 54
Virus
diseases, (1940) 4
chemotherapy, (1944) 321
encephalitis epidemica, (1943) 200, (1944) 221
filter-passing,
aetiology of sarcoma, in, (1940) 4, 7
differentiation, in encephalitis epidemica, (1941-2) 220
ecthyma contagiosum caused by, (1941-2) 217
hepatitis, infective, in, (1944) 34
influenza, variation of strains in, (1941-2) 262
influenza, (1941-2) 3, (1944) 264
pneumonia, atypical, (1944) 41, 170
pneumonitis, in, (1943) 272
poliomyelitis, (1944) 88
rheumatism, as cause of, (1939) 137
swine influenza, (1944) 40
vaccinae, (1940) 579
whooping-cough, (1944) 410
yellow fever, cultivation of, (1941-2) 432
Viruses, disease, as cause of, (1939) 12
Visceral disease, backache simulating, (1943) 142
Viscose rayon workers, carbon disulphide poisoning in, (1943) 365
Viscosimeter, pipette type, (1941-2) 414
Vision
acute alcoholism, effect of, on, (1941-2) 134
aviators, of, (1941-2) 36
loss of power of localization by, (1943) 76
night, (1941-2) 30, (1944) 158
tests for, (1941-2) 31
stereoscopic, in relation to landing of aircraft, (1941-2) 31
Visual
capacity, night flying, for, (1941-2) 30
hallucinations, paraldehyde addiction, in, (1944) 208
Vital azo dye test in rheumatoid arthritis, (1939) 226
Vitalum, use in fixation of fractures, (1941-2) 210
Vitamin A, (1939) 594, (1941-2) 5, 120
absorption,
catarrhal jaundice, in, (1940) 359
liquid paraffin, and, (1940) 585
asthenopia, in, (1940) 202
blood, in, (1940) 116, 585, 592
concentration, (1939) 594
burns, in, (1940) 128
chronic hepatitis, in prognosis of, (1939) 410
coeliac disease, in, (1939) 282
absorption test, (1941-2) 192
colds, for, (1939) 284
Darrier's disease, in, (1941-2) 200
deficiency,
beri-beri, in, (1939) 240
calculus, (1940) 366
dark-adaptation test, (1940) 585
deafness in relation to, (1939) 297
diabetes mellitus, in, (1940) 268
keratomalacia and, (1941-2) 209
mineral oil laxatives and, (1941-2) 426
night-blindness and, (1940) 128
obstructive hepatic jaundice, in, (1941-2) 273
result of, (1939) 14
rheumatoid arthritis, in, (1941-2) 153

CUMULATIVE INDEX

Vitamin A—continued

deficiency—continued

- skin symptoms, (1940) 271
- tuberculosis, in, (1939) 577
- functions of, (1940) 128
- gastric ulcer, in, (1941-2) 327
- growth, effect on, (1940) 128
- hypovitaminosis A, endocrine disorders associated with, (1939) 595
- night-blindness, in, (1939) 595
- phrynodermia, in, (1939) 538
- international unit, (1940) 128
- keratomalacia, in, (1941-2) 209
- keratosis follicularis, in, (1941-2) 200
- miners' requirements, (1941-2) 426
- naso-pharyngeal catarrh, in, (1940) 128
- nephritis, in, (1941-2) 313
- nyctalopia, in, (1940) 128
- official preparations, (1940) 128
- peptic ulcer, in, (1944) 319
- periodontal disease, in, (1940) 128
- preferential solubility in mineral oil, (1941-2) 426

quantitative requirements, (1939) 594 (1940) 128, (1941-2) 426

Sjogren's disease, in, (1939) 595

skin diseases, in, (1940) 128

sources, (1940) 128

therapy, (1940) 128

tonsillitis, in, (1940) 128

toxicity, (1939) 594, (1943) 377

Vitamin B₁ (1941-2) 5

chorea, in, (1941-2) 189

complex, (1940) 114, 128

deafness, in, (1939) 298

deficiency,

alcoholic beri-beri and, (1941-2) 135

dysphagia caused by, (1940) 282

gastro-intestinal disturbances, (1943) 189

hepatic injury due to, (1943) 268

hypertension, in, (1944) 161

mental diseases, in, (1943) 64

multiple neuritis and hepatic cirrhosis, in, (1941-2) 289

peptic ulcer, in, (1939) 466

testing with thiamine, (1944) 204

Wernicke's disease, in, (1940) 69, 287, (1941-2) 369

diabetes mellitus, in, (1941-2) 206

eczema, in, (1940) 285

effects on pigs of deprivation of certain fractions of, (1939) 123

glycogen metabolism and, (1944) 243

hepatic cirrhosis, in, (1943) 268

lichen planus, in, (1941-2) 287

old age, in, (1943) 332

paralysis agitans, in, (1944) 316

pellagra, in, (1941-2) 324

peripheral neuritis, arsenical, in, (1941-2) 410

seborrhoeic dermatoses, in, (1944) 367

thyroid gland function and, (1944) 243

Vitamin B₁₂ (1939) 595, (1941-2) 5, 121

alcoholism, acute, in, (1940) 157

amputation, for pain after, (1940) 168

anaemia, pernicious, nervous symptoms of, in, (1940) 170

appetite, loss of, in, (1940) 129

beri-beri, in, (1939) 149, (1940) 129

oedema of wet, (1943) 378

blood, in, (1940) 115

cardiac complications of alcoholism, in, (1939) 197

cardiac failure with oedema, in, (1940) 129

constipation, atonic, in, (1940) 129

deafness, in, (1940) 256

deficiency, (1940) 114, (1941-2) 422

ankylostomiasis, in, (1939) 219

beri-beri, in, (1939) 239

bisulphite binding substances (B.B.S.) in, (1940) 114

cardiac insufficiency and, (1940) 586

cardiovascular disturbances and, (1941-2) 423

diabetes mellitus, associated with, (1941-2) 206, 422

heart failure, as cause of, (1939) 14

Vitamin B₂—continued

deficiency—continued

metabolism, effect on, of, (1939) 13

pregnancy, in, (1944) 142

toxaemias of, (1940) 479

pyruvic acid and, (1940) 114

delirium tremens, in, (1940) 157

diphtheria, in, (1941-2) 210

disseminated sclerosis, in, (1940) 278

dosage, (1940) 129

dyspnoea, in, (1941-2) 254

excretion of, (1939) 595

functions of, (1940) 129

glucose metabolism, part played in, (1940) 114

gout, in, (1944) 244

heart failure, in, (1941-2) 254

herpes zoster, in, (1939) 374

hyperemesis gravidarum, in, (1944) 334

infantile oedema, in, (1939) 450

infants, effect on growth of, (1941-2) 50

international unit, (1940) 115, 128

irradiation sickness, in, (1940) 505

Korsakow's syndrome, in, (1939) 506, (1940) 497

Landry's paralysis, in, (1939) 398

liver therapy in ulcerative colitis, with, (1939) 287

migraine, in, (1940) 409

nervous diseases, degenerative, intraspinal injection in, (1940) 586

nervous disorders, in, (1939) 596

neuralgia, trigeminal, in, (1940) 423, (1941-2) 314

neuritis, in, (1940) 128, 424, 586

official preparation, (1940) 129

osteoarthritis, in, (1939) 228

pain of ischaemic origin, for, (1939) 596

paralysis, post-diphtheritic, in, (1940) 129

Phycomices blakesleeanae, use of, in estimation, (1940) 115

pink disease, in, (1939) 475, (1940) 464, (1941-2) 50

premature infants, in diet of, (1939) 493

psychoses, in, (1939) 499

quantitative requirements, (1940) 128

shock due to haemorrhage, in, (1943) 338

toxic amblyopia, in, (1939) 244

urinary excretion, (1940) 586

urine, in, (1940) 115

varicose ulcer, in, (1940) 581

vitamin C, relation to, (1940) 587

Vitamin B₂ See also Nicotinic acid

complex, (1939) 596, (1940) 587, (1943) 213

choline as member of, (1941-2) 423

nicotinic acid in disturbed fat absorption, (1939) 596

deficiency, (1940) 115, (1941-2) 424, (1943) 378

excretion of, (1940) 115

functions of, (1940) 129

nicotinic acid in pellagra-like deficiency diseases, (1939) 596

quantitative requirements, (1940) 129

'sore mouth' and, (1941-2) 308

therapy, (1940) 129

urine, in, (1940) 115

Vitamin B₆

amyotrophic lateral sclerosis, in, (1941-2) 428

human nutrition, importance in, (1941-2) 424

hyperemesis gravidarum, in, (1944) 334

muscular dystrophy, in, (1941-2) 428

pseudo-hypertrophic, (1940) 415

neuromuscular diseases, in, (1943) 308

paralysis agitans, in, (1941-2) 322

pellagra, deficiency in, (1943) 378

pyridoxin, isolated as, (1941-2) 423, (1943) 213

therapeutic applications, (1941-2) 424

Vitamin C, (1941-2) 5, 121. See also Ascorbic acid

abortion, in, (1940) 141

acne, in, (1940) 147

anaemias, hypochromic, in, (1940) 130

arthritis, in, (1940) 200

asthma, requirements in, (1941-2) 157

blood, in, estimation of, (1940) 116

concentration, (1939) 597

surgical patients, of, (1940) 592

burns, in, (1939) 268

capillary fragility and haemorrhages, in, (1940) 130

CUMULATIVE INDEX

Vitamin C—*continued*

- cataract, incipient, in, (1940) 130
 - children, normal, requirements for, (1943) 213, 215
 - nutrition of, (1941-2) 49
 - deafness, in, (1939) 297
 - diabetes, nutrition in, (1941-2) 425
 - deficiency, (1941-2) 425; (1943) 213, 378
 - abortion, factor in, (1940) 141
 - arcus senilis caused by, (1939) 293
 - capillary endothelium, effect on, (1939) 54
 - cataract, early, associated with, (1939) 272
 - epileptics, in, (1941-2) 222
 - intestinal disease, in, (1940) 588
 - lesions caused by, (1939) 14
 - tests for, (1940) 115
 - dental sepsis, in, (1940) 256
 - diabetes mellitus, in, (1941-2) 206
 - erythraemia, in, (1941-2) 225
 - febrile states, in, (1940) 130
 - functions, (1940) 129
 - gold therapy reactions, in, (1939) 598
 - haematuria in, (1939) 361
 - haemorrhage, in, (1943) 378
 - hepatic function, influence on, (1940) 587
 - hypervitaminosis C, (1940) 588
 - hypovitaminosis C, intradermal dye test for, (1939) 597
 - infantile diarrhoea, excretion in, (1941-2) 208
 - international unit, (1940) 130
 - intestinal disease, in, (1940) 588
 - lead poisoning, in, (1940) 378
 - milk, in, (1939) 381
 - muscle response to histamine, effect on, (1941-2) 425
 - old age, in, (1943) 332
 - osteoarthritis, in, (1939) 228
 - pellagra, in, (1941-2) 324
 - physiology, (1940) 587
 - placenta, storage by, (1940) 141
 - plasma, in, (1940) 116
 - pregnancy, requirements in, (1944) 22
 - premature infants, in diet of, (1939) 493
 - properties of, (1940) 587
 - quantitative requirements, (1939) 597
 - red blood corpuscles, in, (1940) 116
 - rheumatoid arthritis, in, (1940) 198
 - rose hips and black currants as source of, (1943) 95
 - schoolboys, level in, (1941-2) 425
 - scurvy, in, (1940) 129; (1941-2) 425
 - skin diseases, in, (1940) 588
 - surgical patients, in, (1940) 589
 - therapy, (1939) 598; (1940) 130
 - tonsils, content of, (1939) 563
 - toxic goitre, in, (1939) 354
 - tuberculosis, in, (1941-2) 415
 - pulmonary, (1940) 390
 - urine, excretion in, (1940) 130
 - vitamin B₁, relation to, (1940) 587
 - wound healing, relation to, (1941-2) 13, 268, 425
- ## Vitamin D, (1941-2) 5
- acne, in, (1940) 148
 - children, normal, requirements for, (1943) 213, 216
 - coeliac disease, in, (1939) 282
 - complex, (1940) 589
 - deafness, in, (1939) 298
 - deficiency, in obstructive hepatic jaundice, (1941-1942) 273
 - dental caries and, (1940) 130
 - dental sepsis, in, (1940) 256
 - functions of, (1940) 130
 - international unit, (1940) 130
 - keratoconus, in, (1939) 293
 - large doses, distribution after, (1941-2) 426
 - myopia, in, (1940) 417; (1944) 306
 - official preparations, (1940) 130
 - osteomalacia, in, (1940) 130
 - plasma phosphatase, in, (1940) 116
 - psoriasis, in, (1940) 485
 - quantitative requirements, (1940) 130
 - rheumatoid arthritis, in, (1939) 227
 - rickets, and, (1939) 39, 524; (1940) 130

Vitamin D—*continued*

- spasmophilia and, (1940) 130
 - teeth, calcification of, in, (1940) 130
 - tetany, infantile, and, (1940) 130
 - therapy, (1940) 130
 - thyroid and parathyroid deficiency, in, (1940) 589
- ## Vitamin D₂
- osteomalacia, in, (1940) 589
 - quantitative requirements, (1940) 130
 - rickets, in, (1940) 589
- ## Vitamin D₃
- calciferol, relation to, (1939) 18
 - osteomalacia, in, (1940) 589
 - quantitative requirements, (1940) 130
 - rickets, in, (1940) 589
- ## Vitamin E, (1941-2) 5, 121
- abortion and, (1940) 131, 142; (1943) 16
 - habitual, (1939) 30
 - action of, (1940) 131
 - amyotonia congenita, in, (1940) 131
 - amyotrophic lateral sclerosis, in, (1940) 70, 131, 409, 410, (1941-2) 307, 428, (1944) 89
 - deficiency, (1940) 131
 - nervous diseases, in, (1944) 89
 - nervous system and, (1940) 70
 - pregnancy, in, (1944) 142
 - dosage, (1940) 131
 - fibrositis, in, (1941-2) 230
 - fractures, effect on healing of, (1940) 273
 - hypogalactia, in, (1939) 220
 - miscarriage, in relation to, (1939) 14
 - muscular disease, in, (1941-2) 230
 - muscular dystrophy, in, (1940) 70, 131, 414, (1941-1942) 50, 428
 - myotonia, and, (1941-2) 426
 - nervous disease, in, (1944) 89
 - neuromuscular disease, in, (1941-2) 426, (1943) 308
 - quantitative requirements, (1940) 131
 - tabes dorsalis, in, (1940) 131
 - tocopheryl acetate form of, (1943) 96
- ## Vitamin G (riboflavin), (1940) 115
- ## Vitamin K, (1939) 598, (1941-2) 5, 6, 122, 427
- antenatal administration, effects of, (1944) 246
 - antihæmorrhagic activity, (1940) 590-2
 - bleeding, in post-operative, (1940) 357
 - coeliac disease, in, (1939) 282, (1941-2) 192
 - deficiency,
 - adults, in, (1940) 591
 - anorexia nervosa, in, (1944) 404
 - idiopathic steatorrhoea, associated with, (1941-1942) 192
 - infants, normal and sick, in, (1940) 591
 - new-born, in, (1940) 591
 - post-operative in obstructive jaundice, (1941-2) 273
 - erythroblastosis foetalis, in, (1943) 230
 - haemoptysis, in, (1943) 63
 - prophylaxis, (1943) 230
 - haemorrhage, in relation to, (1939) 54, 598
 - with vitamin P, (1939) 18
 - haemorrhagic disease of new-born, in, (1941-2) 50
 - haemorrhagic states, in, (1940) 4, 6, 16, 31
 - hypoprothrombinaemia, in, (1940) 357, 591; (1943) 230
 - icterus gravis neonatorum, in, (1941-2) 141
 - jaundice, in, (1940) 13
 - labour, in, (1941-2) 428
 - melaena neonatorum, in, (1943) 230
 - menaphthone, official preparation, (1941-2) 113
 - substitute for, (1943) 94
 - naphthoquinone derivatives and, (1940) 590
 - neonatal haemorrhage, in, (1940) 16; (1944) 246
 - phthiocol, properties of, (1940) 590
 - plasma prothrombin,
 - level, effect on, (1943) 378
 - relation in pernicious anaemia, (1941-2) 139
 - pre-operative preparation, in, (1939) 24
 - obstructive jaundice, (1941-2) 273
 - prothrombin, and, (1940) 117, 131, 590
 - level,
 - effect on, (1941-2) 427
 - labour, in, effect on, (1941-2) 428
 - response to, as liver function test, (1944) 288
 - time in new-born, effect on, (1941-2) 427

CUMULATIVE INDEX

Vitamin K—continued

- sources, (1940) 131
- synthetic,
 - coeliac disease treated with, (1941-2) 192
 - hypoproteinaemia, in, (1940) 326, 357
- therapy, (1940) 131
- Vitamin P, (1939) 599; (1941-2) 5, 122
- action of, (1939) 54
- capillary fragility and permeability, effect on, (1941-2) 426
- deficiency, (1941-2) 425
- function of, (1940) 130
- haemorrhage, in relation to, (1939) 599
- haemorrhagic deficiency disorders, in, (1941-2) 241
- psoriasis, in, (1941-2) 362
- purpura, in, (1940) 130; (1941-2) 241
- complicating measles, (1941-2) 302
- Vitamins, (1939) 594; (1941-2) 5, 49, 120, 422; (1944) 404
- children, requirements of, (1943) 213
- deafness, in, (1940) 256
- deficiency,
 - associated with diabetes mellitus, (1941-2) 206
 - coeliac disease, in, (1941-2) 192
 - dermatitis gangrenosa infantum possibly due to, (1939) 300
 - dermatological manifestations, (1939) 311
 - diarrhoea, chronic, causing, (1941-2) 208
 - hepatic injury due to, (1943) 268
 - Hodgkin's disease, in, (1939) 375
 - insulin therapy, during, (1940) 265
 - mental diseases, in, (1943) 64
 - neuritis, multiple, in, (1940) 424
 - hepatic cirrhosis, and, (1941-2) 289
 - neurosyphilis, in, (1939) 447
 - pellagra-like condition in diabetes mellitus, (1941-2) 206
 - skin diseases and, (1943) 377
 - deficiency diseases, and, (1940) 4
 - dental sepsis, in, (1940) 256
 - eye, effects on, (1944) 405
 - fat soluble, (1941-2) 426
 - hypovitaminosis of, in coeliac disease, (1941-2) 192
 - haemostasis, effects on, (1943) 378, (1944) 405
 - mental disease and, (1940) 56
 - official preparations, (1940) 128
 - ophthalmology, in, (1944) 405
 - pregnancy, requirements in, (1939) 29, (1944) 22, 143
 - recent work on, (1940) 114-6
 - therapy, (1940) 585-95
 - diabetes mellitus, in, (1941-2) 206
 - night-blindness, in, (1943) 80
 - old age, in, (1943) 332
 - ophthalmology, in, (1943) 80, 147; (1944) 405
 - survey of, (1939) 18
 - water-soluble, (1941-2) 422
- Vitelline vascular system, intestinal obstruction caused by, (1940) 354
- Vitex peduncularis*, blackwater fever treated by tincture of, (1943) 144
- Vocal cords, bilateral abductor paralysis of, treatment of, (1939) 92
- Voice, effect of helium-oxygen mixture on, (1941-2) 335
- Volkman's ischaemic contracture
 - lower limb, of, (1940) 275
 - occlusion of brachial artery causing, (1940) 195
- Vollmer patch test, tuberculosis, for, (1940) 568
- Vomiting, (1939) 599
 - epidemic nausea and vomiting, (1939) 599
 - sodium chloride in treatment, (1939) 599
 - stilboestrol therapy causing, (1944) 26
 - winter, (1941-2) 232
- Von Gierke's disease, (1940) 314
- Von Hippel's disease, X-ray therapy, (1940) 385
- Von Ritter's disease, sulphapyridine in, (1940) 260
- Vulva
 - adenocarcinoma of, (1943) 379
 - disease, (1940) 132, 592; (1941-2) 429; (1944) 405

Vulva—continued

- epithelioma, (1941-2) 430
- fusion, dangers of, (1941-2) 430
- granuloma, infective, (1940) 593
- kraurosis, oestrogenic treatment, (1940) 593
- leucoplakia,
 - mercury sulphide tattoo, (1941-2) 430
 - oestrogen treatment of, (1939) 600
- post-partum labial and paravaginal haematoma, (1940) 593
- pregnancy, mycotic infections during, (1940) 594
- pruritus,
 - magnesium sulphate injections in, (1940) 593
 - stilboestrol in treatment, (1940) 132, (1941-2) 430
- tumours, (1941-2) 430
 - benign, (1943) 379
- vagina diseases, and, (1939) 600
- carcinoma, (1939) 601
- melanoma, (1939) 601
- vagina, absence or obliteration of, (1939) 600
- vaginal hernia, posterior, (1939) 601
- vaginitis,
 - aetiology and treatment, (1939) 600
- vioform in treatment, (1939) 600
- Vulvar fusion, (1941-2) 430
- Vulvovaginitis
 - children, in, (1940) 319; (1941-2) 108
 - gonococcal, (1940) 319, (1943) 91, 226
 - treatment, (1940) 319
 - gonococcal, (1941-2) 108
 - treatment, (1940) 319
 - acidulation of vagina, (1940) 320
 - diethylstilboestrol, (1940) 319
 - mandelic acid and oestrogen, (1940) 320
 - silver picrate suppositories, (1940) 320
 - sulphonamide, (1940) 91
 - Trichomonas vaginalis* causing, (1944) 406
 - treatment of, (1939) 403, 600
- Vulvovagino-cervicitis, chrysotherapy causing, (1944) 405

W

- Waelisch urethritis, (1939) 156
- Wangensteen tube, in treatment of intestinal obstruction, (1940) 12
- War *See also* Air-raids; Air-raid casualties, Aviation, Aviation medicine; Effort syndrome; Flying, Forces, Recruits, Soldiers
- abdominal wounds, (1944) 267
- air-raid casualties, surgery of, (1941-2) 265
- alcoholism and, (1940) 280
- anaemia in, (1944) 133
 - nutritional, (1944) 131
- anaesthesia, (1943) 8
- armour, use of, (1943) 8
- blast injuries, (1941-2) 297
- blood transfusion in, (1943) 157
- burns, treatment of, (1941-2) 179
- cerebrospinal fever in, (1944) 11
- deficiency disease in, (1944) 9
- digestive disease in, (1944) 214
- diphtheria in, (1944) 10
- disease in the present, (1944) 9
- drug addiction and, (1940) 280
- drug shortage and, (1941-2) 111; (1943) 5, 82, 93
- drugs, supply of, (1940) 127
- dysentery and diarrhoea in, (1944) 210
- dyspepsia in, (1944) 214
 - armed Forces, (1941-2) 214
- enteric fever in, (1944) 11
- epidemics resulting from, (1940) 75
- epidemiological trends in, (1941-2) 62
- epilepsy, feigned, in, (1940) 400
- food in, (1943) 214-6
- foot disease and military service, (1941-2) 232
- foot strain in, (1944) 236
- functional nervous disease in, (1940) 7
- gastro-intestinal disease and, (1941-2) 214
- head injuries in, (1943) 8, 178, 250
- heart disease and, (1941-2) 244; (1943) 232
- infective disease in, (1944) 10, 57
- influence of, on the progress of medicine, (1940) 3

CUMULATIVE INDEX

War—continued

- influenza in, (1941-2) 263; (1944) 10
- injuries, civilians and, (1944) 343
- malaria and, (1940) 75; (1943) 82, 277
- malinger, (1944) 79
- mental disease in, (1943) 68, 314; (1944) 78
- influence on, (1941-2) 363
- morale, (1943) 69
- neurosis, (1940) 61; (1941-2) 85; (1944) 342-5
 - air-raids, effects of, (1944) 341
 - civilians and war injuries, (1944) 343
 - psychopathic disposition, (1944) 342
 - treatment, (1943) 68, (1944) 343
- psychiatry in, (1941-2) 85, (1943) 68; (1944) 78
- psychoneurosis in, (1940) 61, (1941-2) 85, 363
- public health in, (1944) 1
- rickets, prevention of, (1943) 328
- scabies and, (1943) 340, 343
- skin diseases in, (1943) 348
- Spanish Civil, and its lessons, (1940) 9
- stimulus to medical research, (1940) 3
- surgery, (1940) 9, (1941-2) 8, (1943) 8, (1944) 16-9
 - restorative or plastic, (1941-2) 12
 - value of records in, (1941-2) 8
- syphilis and, (1943) 87, 358
- tuberculosis and, (1940) 96, (1944) 9
 - incidence of, (1941-2) 4
- typhus fever in, (1944) 11
- venereal disease in, (1944) 10, 102
- wounded, rehabilitation of, (1943) 10
- wounds, (1943) 247, (1944) 16
 - chemotherapy of, (1941-2) 10
 - management of, (1941-2) 10
 - sulphonamides, use of, (1944) 111
- Warts, (1944) 373
- eyelids, on, (1939) 338
- mental deficiency associated with, (1939) 431
- plantar, X-rays and radium therapy for, (1941-2) 393
- radon gas in, (1939) 514
- urea therapy, (1940) 533
- Wasp sting, death caused by, (1943) 144
- Wassermann reaction, (1943) 87
- Boerner-Lukens modification of, (1940) 547
- glandular fever, in, (1943) 88
- malaria, in, (1943) 88, 355
- Meinicke flocculation test, comparison with, (1940) 547
- pneumonia, in, (1943) 89
- respiratory infections, in, (1943) 88
- vaccinia, in, (1943) 88
- Water
 - balance,
 - allergy, in, (1940) 159
 - epilepsy, in, (1944) 226, 228, 230
 - pituitary gland and, (1940) 261
 - surgical shock, in, (1940) 527
 - test, for epileptic convulsions, (1944) 228
 - metabolism,
 - epilepsy, in, (1944) 226
 - hypothalamus and, (1940) 66
 - paratyphoid B infection from, (1944) 224
 - pyrogen-free, for intravenous transfusion, (1940) 356
- Waterhouse-Friderichsen syndrome, (1941-2) 132
- meningococcal septicaemia associated with, (1941-1942) 186
- Weaning
 - avoidance of unnecessary, (1944) 260
 - premature, (1944) 261
- Weber-Christian syndrome, (1943) 208
- Weight, progressive increase, in Graves's disease, (1943) 223
- Weil's disease, (1939) 389. *See also* Spirochaetosis icterohaemorrhagica
 - occupational hazard, as, (1943) 255
- Weil-Felix test, tick-bite fever, in, (1940) 85
- Werlhof's disease, (1939) 547
- Werner's syndrome, (1943) 298
- Wernicke's disease (encephalitis haemorrhagica superior), (1939) 196; (1940) 69, 287
- vitamin B₁ deficiency and, (1940) 69
- Wernicke's polio-encephalitis, vitamin B deficiency associated with, (1941-2) 369
- Wesselow and Griffiths' test, diabetes mellitus, in, (1941-2) 206
- Whale-oil, use in tropical ulcer, (1941-2) 413
- Wheat-germ oil, (1940) 131. *See also* Vitamin E
 - abortion treated with, (1940) 142
 - lichen planus caused by, (1941-2) 286
 - muscular dystrophy treated with, (1940) 414
- Whooping-cough, (1939) 601; (1941-2) 431; (1943) 180, 379; (1944) 406-10
 - bacteriology, (1939) 602; (1944) 406
 - brain lesions,
 - associated with convulsions, (1943) 379
 - psychopathic disturbances, (1944) 407
 - carriers, adult, (1939) 601
 - clinical aspects of, (1944) 409
 - complications, (1940) 594
 - convulsions, (1939) 602
 - encephalitis and epilepsy, (1940) 594
 - pneumonia, sulphapyridine therapy in, (1941-2) 431
 - sequelae, and, (1941-2) 431; (1944) 407
 - virus infection, (1939) 425
- diagnosis, (1939) 79, 602, (1941-2) 68
 - lymphocyte count, differential, in, (1943) 380
- nasopharyngeal cultures and cough plate cultures, (1944) 407
- immunization,
 - children, in, (1944) 408
 - intranasal, (1944) 408
- intradermal tests, (1944) 408
- prophylaxis, (1940) 595, (1941-2) 69, (1944) 408
 - antigen, (1941-2) 431
 - specific, (1939) 78
 - vaccines, (1939) 603
- susceptibility,
 - intracutaneous test, (1941-2) 431
 - skin test, (1940) 595
- treatment, (1941-2) 68, 431, (1944) 408-10
 - airplane flights, (1944) 408
 - altitude and low atmospheric pressures, (1944) 408
 - antigen, (1941-2) 431
 - detoxified, (1940) 595
 - intranasal soluble, (1941-2) 431
 - serum, (1940) 595
 - antipertussis, (1943) 380
 - immune, (1943) 380
 - sulphanilamide, (1939) 603
 - ultra-violet irradiation, (1940) 595
 - vaccines, (1943) 55, 380
 - vitamin C, (1939) 603
- virus,
 - inactivation of, (1944) 410
 - surface-active agents, by, (1944) 410
- vitamin D deficiency, (1939) 604
- Widal test, (1941-2) 63
- Wide-field X-ray therapy, (1940) 104
- Williams's apparatus for flying aptitude test, (1941-2) 29
- Wilms's tumour, (1943) 260
 - kidney, of, (1940) 365
- Wilson's disease, (1943) 241
- Winter
 - diet in, (1943) 216
 - vomiting, (1941-2) 232
- Wintergreen, oil of, fatal poisoning by, (1941-2) 409
- Woldman test, (1941-2) 273
- Wolff-Parkinson-White syndrome, (1943) 131
- Women
 - anaemia, nutritional, in, (1944) 131
 - industry, in, (1944) 259
- Woods, irritant, dermatitis caused by, (1941-2) 203
- Workmen's Compensation, industrial psychiatry and, (1943) 69
- Wound
 - revision, (1940) 9
 - shock, (1941-2) 39. *See also* Shock
- Wounded
 - evacuation by air, (1943) 8
 - transport of, in war, (1940) 9
- Wounds, (1941-2) 263
 - abdominal, (1943) 10, 247; (1944) 267
 - amnioplastin, use of, (1941-2) 264

CUMULATIVE INDEX

Wounds—continued

- anaesthesia, (1943) 8
- aseptic pus, (1940) 349
- bacteriology of, (1941-2) 267
- chemotherapy of, (1941-2) 10, 265
- cross-infection, streptococcal, in, (1943) 248
- dressings, (1940) 349; (1941-2) 263
 - bandage, new transparent, (1940) 349
 - Cellophane, (1940) 349
 - cod-liver oil, (1940) 350
 - petroleum jelly, (1941-2) 264
 - tulle gras, (1941-2) 263
- embryonic extract, use of, (1940) 351
- epicutan, use of, (1940) 351
- first aid, essentials of, (1944) 271
- gunshot, heart, of, (1943) 236
- haemolytic streptococcal infection, (1940) 347
- haemostasis, mechanism of, (1941-2) 268
- healing, (1941-2) 113; (1943) 9, 248
 - delayed, vitamin C deficiency cause of, (1939) 14
 - nutrition, and, (1941-2) 13
 - sulphathiazole, importance of, (1944) 269
 - vitamin C,
 - and serum protein in, (1941-2) 268
 - role of, (1941-2) 425
- infected, (1940) 350-3, (1941-2) 265
 - chemotherapy, (1941-2) 265
 - early precautions, (1941-2) 266
 - silk sutures in, (1941-2) 266
- treatment,
 - closed-plaster, (1940) 350; (1941-2) 267
 - cystine hydrochloride, (1941-2) 268
 - hypertonic sodium sulphate solution, (1940) 351
 - acriflavine and, (1941-2) 268
 - propamidine, (1944) 269
 - sulphathiazole, (1944) 269
 - sulphonamides, (1941-2) 266
 - local, (1944) 268
 - zinc peroxide, (1941-2) 267
- intrathoracic, (1943) 9, 247
- morphine, administration of, (1944) 271
- penetrating, of abdomen, (1940) 347
- rest, importance of, (1940) 9
- serum protein concentration in, (1941-2) 263
- sulphonamides as antiseptics, (1941-2) 114
- surgical, (1943) 9, 247
- toilet of, (1944) 271
- treatment, (1944) 269
 - antiseptics, (1943) 248, (1944) 270
 - assessment of modern methods, (1944) 273
 - closed-plaster, (1940) 350
 - bacteriology of wounds treated by, (1941-2) 267
 - cod-liver oil and allied substances, (1940) 350, (1943) 248
 - electrolysis, (1943) 249
 - hypertonic sodium sulphate solution, (1940) 351
 - immediate, (1940) 9
 - maggot therapy, (1940) 352
 - plaster of Paris casts, 'windowed' unpadded, (1941-2) 265
 - propamidine, (1944) 322
 - soap and water, value of, (1944) 271
 - sulphanilamide, (1943) 9, 305
 - local, (1940) 132, 351, (1944) 270
 - sulphonamides, (1940) 10
 - local, (1941-2) 114
 - surgical, (1944) 16
 - vitamin C in relation to, (1940) 589
 - zinc peroxide in, (1940) 349
- Wrist
 - chromoblastomycosis on, (1941-2) 233
 - dislocation and fracture, (1943) 194
 - fracture, (1941-2) 211
- Wuchereria bancrofti*, eye, infestation of, (1944) 233

X

- Xanthine compounds, coronary disease treated with, (1943) 127
- Xanthoma, (1940) 228
 - cutaneous, and the melanomas, (1940) 534
 - diabeticorum, with lipodystrophia, (1940) 263
 - larynx, of, (1943) 42

- Xanthomatosis, bony, (1940) 228
- Xanthomatous biliary cirrhosis, (1941-2) 287
- Xenopus laevis*, (1941-2) 358
- Xenopus test, diagnosis of pregnancy, in, (1941-2) 358
- Xerophthalmia, vitamin-A deficiency in, (1940) 116
- Xerostomia, nicotinic acid deficiency causing, (1941-2) 424
- Xiphophorus helleri*, as test animals for endocrine substances, (1940) 523
- X-ray examination, (1941-2) 371, (1944) 355-8. See also Mass radiography
 - adenoids, of, (1940) 151
 - adrenal tumour, of, (1940) 155
 - air-raid casualties, in, (1941-2) 371
 - alimentary tract, of, (1944) 356
 - angiography, cerebral, (1940) 103
 - aortic arch, right-sided, of, (1941-2) 246
 - arteriography, cerebral, (1940) 103
 - articular cartilage, of, (1940) 102
 - backache, in, (1943) 142
 - biliary dyskinesia, in, (1941-2) 233
 - blast injury of lung, in, (1943) 271
 - bronchiectasis, in, (1944) 67
 - chronic, (1940) 233
 - calculus, renal, of, (1940) 368
 - cardiac circulation, in, (1944) 355
 - cerebral tumour, of, (1941-2) 175
 - cineradiography, (1940) 98-101
 - coeliac axis, calcification of, in, (1941-2) 153
 - contrast media, (1940) 502; (1941-2) 371, (1943) 321
 - fatal diodrast (diodone) administration, (1944) 355
 - coronary artery disease, in, (1941-2) 146
 - craniolacunia, in, (1944) 233
 - C rohn's disease, in, (1941-2) 199
 - cysticercosis, in, (1941-2) 200
 - brain, of, (1941-2) 200
 - diaphragmatic wounds, in, (1943) 322
 - duodenitis, in, (1943) 321
 - dyspepsia in soldiers, in, (1941-2) 215
 - embolism, pulmonary, in, (1944) 296
 - encephalography, (1940) 102
 - endocrine disease, in, (1944) 357
 - erythema nodosum, in, (1943) 205
 - erythraemia, in, (1940) 297; (1943) 206
 - fat embolism, in, (1943) 337
 - fluorescent screen, (1944) 355
 - foreign bodies, of, (1941-2) 371
 - localization of, (1944) 355
 - gall-bladder, of, (1940) 503
 - gas gangrene, in, (1940) 308
 - gastric carcinoma, in, (1940) 544
 - gastritis, in, (1943) 221
 - gastroscopy and, comparative values of, (1943) 202
 - head injury, in, (1944) 357
 - heart chambers, visualization of, (1940) 503
 - Hodgkin's disease, in, (1943) 244
 - interauncular septum, defects of, (1941-2) 247
 - intervertebral disks, of, (1943) 350
 - protrusion of, (1940) 538
 - intestinal obstruction, acute, in, (1941-2) 271
 - intussusception, in, (1940) 353
 - joints, of, (1940) 102
 - kidney, of, (1941-2) 372; (1943) 322
 - kymography, (1940) 101, (1943) 321
 - labour, in, (1941-2) 280
 - lipiodol, intracranial collections of, (1940) 502
 - lungs, of, (1943) 319-22
 - Lysholm grid, (1940) 103
 - mass miniature radiography, (1940) 94, 103, 106; (1941-2) 75, 292; (1943) 2, 319, 324
 - Australian children, in, (1944) 356
 - technique, (1944) 356
 - maxillary antrum, of, (1941-2) 127
 - myelography with iodized oil, (1941-2) 371
 - nervous system, in, (1941-2) 371
 - neuroblastoma sympathetum, in, (1943) 354
 - pancreatic calculi, of, (1943) 296
 - peptic ulcers in soldiers, of, (1941-2) 215
 - per-abrodil (diodone), in poisoning by, (1940) 503
 - pituitary fossa, of, (1944) 357

CUMULATIVE INDEX

X-ray examination—*continued*

planigraphy, (1940) 101
 pleural effusions, in, (1941-2) 352
 Plummer-Vinson syndrome, in, (1941-2) 128
 pregnancy, in, (1941-2) 280
 prostate, of, (1941-2) 360
 pyelography. *See* Pyelography
 renal tract, of, (1944) 357
 respiratory tract, of, (1944) 356
 roentgen-cinematography, (1944) 355
 sciatica, in, (1944) 362
 scurvy, in, (1940) 517
 semilunar cartilages, of, (1940) 102
 silicosis, in, (1943) 338
sinuses, nasal accessory, of, (1941-2) 127
 skeletal system, of, (1941-2) 371
 skull, of, (1944) 357
 sodium thorium tartrate in, (1941-2) 371
 soft-tissue radiography, (1940) 102
 pregnancy, in, (1941-2) 280
 spinal cord, of, (1941-2) 371
 stratigraphy, (1940) 101
 suprasternal bones, of, (1941-2) 371
 syphilis, congenital, in, (1943) 356
 tomography, (1940) 101
 tuberculo-silicosis, in, (1941-2) 390
 tuberculosis, pulmonary, in, (1940) 6; (1941-2) 292; (1943) 2, 319, 324
 urinary tract, of, (1940) 370
 uroselectan B in, (1941-2) 371
 ventriculography, (1940) 102
X-ray therapy, (1941-2) 372
 acne vulgaris, in, (1944) 121
 adenoids, of, (1939) 187
 angiomatosis retinae, in, (1940) 385
 baths, regional X-ray, (1940) 105
 bladder, malignant growths, of, (1940) 208
 blood, of, toxic effects on, (1941-2) 372
 bone, of, benign giant-celled tumour of, (1941-2) 172; (1943) 160
 bronchiectasis, in, (1939) 265
 cancer, in, (1939) 28, 271; (1941-2) 372
 cervix, of, (1940) 504
 fever therapy combined with, (1944) 175
 larynx, of, (1943) 262
 skin, of, (1941-2) 394
 carcinoma, of,
 breast, (1939) 263; (1941-2) 176; (1944) 167
 bronchiogenic, (1941-2) 374
 cervix uteri, (1939) 589; (1941-2) 373, 419
 vesical, (1939) 242
 rectum, (1940) 507; (1941-2) 375
 skin, (1941-2) 394
 concrete as protective material, (1940) 502
 contact therapy, (1940) 105
 Chaoul's, (1940) 105
 deep,
 bronchial carcinoma, in, (1944) 67
 malignant bronchial tumour, harmful effects on, (1941-2) 372
 dermatology, dosage in, (1940) 504
 diabetes mellitus and hypertension, in, (1943) 152
 dosage, estimation of, (1944) 358
 entire body, irradiation of, (1944) 358
 epilation by, (1940) 328
 exanthem, generalized, after, (1940) 505
 ganglion, of, (1941-2) 243
 gas gangrene, in, (1944) 241
 granuloma pyogenicum, in, (1940) 532
 herpes zoster, in, (1941-2) 256
 high voltage, (1940) 105; (1941-2) 373
 rheumatoid arthritis, in, (1941-2) 373
 Hodgkin's disease, in, (1939) 375; (1940) 344; (1943) 244; (1944) 253
 pregnancy, in, (1944) 252
 hypertension, in, (1940) 214
 injuries from, (1940) 505
 intestine, small, effect on, (1941-2) 372
 Jensen's rat sarcoma, in, (1941-2) 372
 keloid, in, (1943) 256
 laryngeal papilloma, in, (1943) 43

X-ray therapy—*continued*

leukaemia, in, (1940) 6, 384
 'spray' technique, (1941-2) 285
 Lindau's disease, in, (1940) 385
 lupus erythematosus disseminatus, in, (1940) 396
 lymph glands, in, (1940) 6
 lymphopathia venereum, in, (1940) 399
 mastitis, chronic interstitial, in, (1940) 104
 menorrhagia, in, (1939) 430
 myeloid sarcoma, of, (1941-2) 172
 osteoclastoma, of, (1941-2) 172
 parotid gland tumours, of, (1943) 299
 parotitis, acute suppurative, in, (1940) 434
 pituitary adenomas, of, (1940) 467
 plantar warts, of, (1939) 539; (1941-2) 393
 pneumonia, in, (1940) 474
 lobar, (1941-2) 355
 psoriasis of nails, in, (1941-2) 362
 radium, and, in cancer of cervix, (1940) 504
 regional X-ray baths, (1940) 105
 scleroderma, in, (1940) 517
 serum cholesterol level, effect on, (1941-2) 372
 short distance therapy, (1940) 105
 sinusitis, in, (1940) 145; (1941-2) 127
 skin diseases, in, (1941-2) 373
 malignant, (1944) 374
 spleen, in, (1940) 6
 sulphanilamide, hypersensitivity to, after, (1940) 505
 superficial, (1940) 104
 super high-voltage, (1940) 105, 208
 uraemia after, (1940) 384
 von Hippel's disease, in, (1940) 385
 wide-field, (1940) 104
 Scott's, (1940) 104
X-rays
 blood pressure, effect on, (1939) 250
 mitosis, effect on, (1941-2) 416
 occupational exposure, effects of, (1944) 388
 tumours, radio-sensitivity of, (1941-2) 372
 Xylose clearance test, kidney function, of, (1940) 118

Y

Yaws, (1939) 604
 syphilis as form of, (1939) 604
 Yeast in tropical megalocytic anaemia, (1939) 204
 Yellow fever, (1939) 604; (1941-2) 99; (1943) 5, 85, 381
 Anglo-Egyptian Sudan epidemic, (1943) 381
 brain changes in, (1939) 604
 control of, (1939) 145
 distribution, (1944) 99
 epidemiology and immunity, (1943) 381
 immunity, mouse-protection tests, (1944) 410
 Kordofan province, in, (1943) 381
 liver changes after burns, diagnosis from, (1939) 605
 mouse protection tests, (1944) 410
 prophylaxis, (1940) 596; (1944) 99
 combined, against smallpox and, (1939) 605; (1940) 596
 serum treatment, (1943) 381
 virus, cultivation of, (1941-2) 432

Z

Zephiran as antiseptic, (1939) 385
 Zinc globulin insulin, (1940) 267
 Zinc peroxide
 antiseptic action of, (1939) 474
 radionecrotic ulcers treated with, (1941-2) 372
 surgical infections, use in, (1941-2) 267
 ulcers, chronic undermining, (1940) 572
 wounds treated with, (1940) 349
 Zinc protamine insulin, (1940) 265
 diabetes mellitus, in, (1941-2) 206
 diabetes with tuberculosis, for, (1941-2) 206
 non-diabetic individuals, effect on, (1940) 452
 Zymonema dermatitidis, (1940) 209

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